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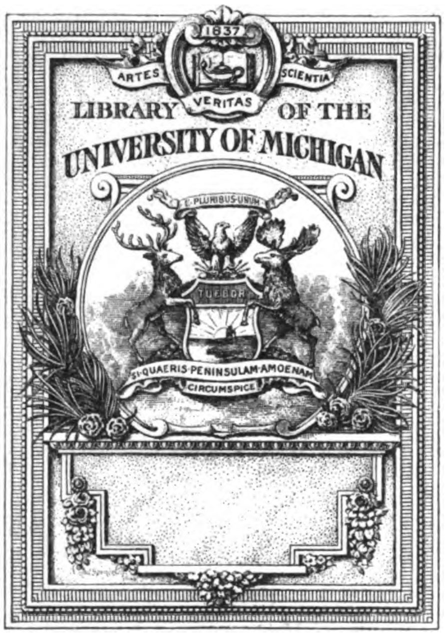
Philosophical Transactions of the Royal Society of London

Royal Society (Great Britain), JSTOR (Organization)



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TRANSACTIONS

OF THE

ROYAL SOCIETY OF LONDON.

SERIES B

CONTAINING PAPERS OF A BIOLOGICAL CHARACTER.

FOR THE YEAR 1897.

VOL. 188.

LONDON:
PRINTED BY HARRISON AND SONS, ST. MARTIN'S LANE, W.C,
Printers in Ordinary to Her Majesty.
1897.

ADVERTISEMENT.

The Committee appointed by the *Royal Society* to direct the publication of the *Philosophical Transactions* take this opportunity to acquaint the public that it fully appears, as well from the Council-books and Journals of the Society as from repeated declarations which have been made in several former *Transactions*, that the printing of them was always, from time to time, the single act of the respective Secretaries till the Forty-seventh Volume; the Society, as a Body, never interesting themselves any further in their publication than by occasionally recommending the revival of them to some of their Secretaries, when, from the particular circumstances of their affairs, the *Transactions* had happened for any length of time to be intermitted. And this seems principally to have been done with a view to satisfy the public that their usual meetings were then continued, for the improvement of knowledge and benefit of mankind: the great ends of their first institution by the Royal Charters, and which they have ever since steadily pursued.

But the Society being of late years greatly enlarged, and their communications more numerous, it was thought advisable that a Committee of their members should be appointed to reconsider the papers read before them, and select out of them such as they should judge most proper for publication in the future *Transactions;* which was accordingly done upon the 26th of March, 1752. And the grounds of their choice are, and will continue to be, the importance and singularity of the subjects, or the advantageous manner of treating them; without pretending to answer for the certainty of the facts, or propriety of the reasonings contained in the several papers so published, which must still rest on the credit or judgment of their respective authors.

It is likewise necessary on this occasion to remark, that it is an established rule of the Society, to which they will always adhere, never to give their opinion, as a Body, upon any subject, either of Nature or Art, that comes before them. And therefore the thanks, which are frequently proposed from the Chair, to be given to the authors of such papers as are read at their accustomed meetings, or to the persons through whose hands they received them, are to be considered in no other light than as a matter of civility, in return for the respect shown to the Society by those communications. The like also is to be said with regard to the several projects, inventions, and curiosities of various kinds, which are often exhibited to the Society; the authors whereof, or those who exhibit them, frequently take the liberty to report, and even to certify in the public newspapers, that they have met with the highest applause and approbation. And therefore it is hoped that no regard will hereafter be paid to such reports and public notices; which in some instances have been too lightly credited, to the dishonour of the Society.

1897.

LIST OF INSTITUTIONS ENTITLED TO RECEIVE THE PHILOSOPHICAL TRANSACTIONS OR PROCEEDINGS OF THE ROYAL SOCIETY.

Institutions marked A are entitled to receive Philosophical Transactions, Series A, and Proceedings.
„ „ B „ „ „ „ Series B, and Proceedings.
„ „ AB „ „ „ „ Series A and B, and Proceedings.
„ „ *p* „ „ Proceedings only.

America (Central).
Mexico.
- *p.* Sociedad Científica "Antonio Alzate."

America (North). (See UNITED STATES and CANADA.)

America (South).
Buenos Ayres.
- AB. Museo Nacional.

Caracas.
- B. University Library.

Cordova.
- AB. Academia Nacional de Ciencias.

Demerara.
- *p.* Royal Agricultural and Commercial Society, British Guiana.

La Plata.
- B. Museo de La Plata.

Rio de Janeiro.
- *p.* Observatorio.

Australia.
Adelaide.
- *p.* Royal Society of South Australia.

Brisbane.
- *p.* Royal Society of Queensland.

Melbourne.
- *p.* Observatory.
- *p.* Royal Society of Victoria.
- AB. University Library.

Sydney.
- *p.* Australian Museum.
- *p.* Geological Survey.
- *p.* Linnean Society of New South Wales.
- AB. Royal Society of New South Wales.
- AB. University Library.

Austria.
Agram.
- *p.* Jugoslavenska Akademija Znanosti i Umjetnosti.
- *p.* Societas Historico-Naturalis Croatica.

Austria (continued).
Brünn.
- AB. Naturforschender Verein.

Gratz.
- AB. Naturwissenschaftlicher Verein für Steiermark.

Innsbruck.
- AB. Das Ferdinandeum.
- *p.* Naturwissenschaftlich - Medicinischer Verein.

Prague.
- AB. Königliche Böhmische Gesellschaft der Wissenschaften.

Trieste.
- B. Museo di Storia Naturale.
- *p.* Società Adriatica di Scienze Naturali.

Vienna.
- *p.* Anthropologische Gesellschaft.
- AB. Kaiserliche Akademie der Wissenschaften.
- *p.* K.K. Geographische Gesellschaft.
- AB. K.K. Geologische Reichsanstalt.
- B. K.K. Naturhistorisches Hof-Museum.
- B. K.K. Zoologisch-Botanische Gesellschaft.
- *p.* Oesterreichische Gesellschaft für Meteorologie.
- A. Von Kuffner'sche Sternwarte.

Belgium.
Brussels.
- B. Académie Royale de Médecine.
- AB. Académie Royale des Sciences.
- B. Musée Royal d'Histoire Naturelle de Belgique.
- *p.* Observatoire Royal.
- *p.* Société Belge de Géologie, de Paléontologie, et d'Hydrologie.
- *p.* Société Malacologique de Belgique.

Ghent.
- AB. University.

Belgium (continued).
Liége.
AB. Société des Sciences.
p. Société Géologique de Belgique.
Louvain.
B. Laboratoire de Microscopie et de Biologie Cellulaire.
AB. Université.

Canada.
Hamilton.
p. Hamilton Association.
Montreal.
AB. McGill University.
p. Natural History Society.
Ottawa.
AB. Geological Survey of Canada.
AB. Royal Society of Canada.
Toronto.
p. Astronomical and Physical Society.
p. Canadian Institute.
AB. University.

Cape of Good Hope.
A. Observatory.
AB. South African Library.

Ceylon.
Colombo.
B. Museum.

China.
Shanghai.
p. China Branch of the Royal Asiatic Society.

Denmark.
Copenhagen.
AB. Kongelige Danske Videnskabernes Selskab.

Egypt.
Alexandria.
AB. Bibliothèque Municipale.

England and Wales.
Aberystwith.
AB. University College.
Bangor.
AB. University College of North Wales.
Birmingham.
AB. Free Central Library.
AB. Mason College.
p. Philosophical Society.
Bolton.
p. Public Library.
Bristol.
p. Merchant Venturers' School.
AB. University College.
Cambridge.
AB. Philosophical Society.
p. Union Society.

England and Wales (continued).
Cooper's Hill.
AB. Royal Indian Engineering College.
Dudley.
p. Dudley and Midland Geological and Scientific Society.
Essex.
p. Essex Field Club.
Falmouth.
p. Royal Cornwall Polytechnic Society.
Greenwich.
A. Royal Observatory.
Kew.
B. Royal Gardens.
Leeds.
p. Philosophical Society.
AB. Yorkshire College.
Liverpool.
AB. Free Public Library.
p. Literary and Philosophical Society.
A. Observatory.
AB. University College.
London.
AB. Admiralty.
p. Anthropological Institute.
AB. British Museum (Nat. Hist.).
AB. Chemical Society.
A. City and Guilds of London Institute.
p. "Electrician," Editor of the.
B. Entomological Society.
AB. Geological Society.
AB. Geological Survey of Great Britain.
p. Geologists' Association.
AB. Guildhall Library.
A. Institution of Civil Engineers.
p. Institution of Electrical Engineers.
A. Institution of Mechanical Engineers.
A. Institution of Naval Architects.
p. Iron and Steel Institute.
AB. King's College.
B. Linnean Society.
AB. London Institution.
p. London Library.
A. Mathematical Society.
p. Meteorological Office.
p. Odontological Society.
p. Pharmaceutical Society.
p. Physical Society.
p. Quekett Microscopical Club.
p. Royal Agricultural Society.
A. Royal Astronomical Society.
B. Royal College of Physicians.
B. Royal College of Surgeons.

England and Wales (continued).

London (continued).

- *p.* Royal Engineers (for Libraries abroad, six copies).
- AB. Royal Engineers. Head Quarters Library.
- *p.* Royal Geographical Society.
- *p.* Royal Horticultural Society.
- AB. Royal Institution of Great Britain.
- B. Royal Medical and Chirurgical Society.
- *p.* Royal Meteorological Society.
- *p.* Royal Microscopical Society.
- *p.* Royal Statistical Society.
- AB. Royal United Service Institution.
- AB. Society of Arts.
- *p.* Society of Biblical Archæology.
- *p.* Society of Chemical Industry (London Section).
- *p.* Standard Weights and Measures Department.
- AB. The Queen's Library.
- AB. The War Office.
- AB. University College.
- *p.* Victoria Institute.
- B. Zoological Society.

Manchester.

- AB. Free Library.
- AB. Literary and Philosophical Society.
- *p.* Geological Society.
- AB. Owens College.

Netley.

- *p.* Royal Victoria Hospital.

Newcastle.

- AB. Free Library.
- *p.* North of England Institute of Mining and Mechanical Engineers.
- *p.* Society of Chemical Industry (Newcastle Section).

Norwich.

- *p.* Norfolk and Norwich Literary Institution.

Nottingham.

- AB. Free Public Library.

Oxford.

- *p.* Ashmolean Society.
- AB. Radcliffe Library.
- A. Radcliffe Observatory.

Penzance.

- *p.* Geological Society of Cornwall.

Plymouth.

- B. Marine Biological Association.
- *p.* Plymouth Institution.

Richmond.

- A. "Kew" Observatory.

Salford.

- *p.* Royal Museum and Library.

England and Wales (continued).

Stonyhurst.

- *p.* The College.

Swansea.

- AB. Royal Institution.

Woolwich.

- AB. Royal Artillery Libra[illegible]

Finland.

Helsingfors.

- *p.* Societas pro Fauna et Flora Fennica.
- AB. Société des Sciences.

France.

Bordeaux.

- *p.* Académie des Sciences.
- *p.* Faculté des Sciences.
- *p.* Société de Médecine et de Chirurgie.
- *p.* Société des Sciences Physiques et Naturelles.

Caen.

- *p.* Société Linnéenne de Normandie.

Cherbourg.

- *p.* Société des Sciences Naturelles.

Dijon.

- *p.* Académie des Sciences.

Lille.

- *p.* Faculté des Sciences.

Lyons.

- AB. Académie des Sciences, Belles-Lettres et Arts.
- AB. Université.

Marseilles.

- AB. Faculté des Sciences.

Montpellier.

- AB. Académie des Sciences et Lettres.
- B. Faculté de Médecine.

Nantes.

- *p.* Société des Sciences Naturelles de l'Ouest de la France.

Paris.

- AB. Académie des Sciences de l'Institut.
- *p.* Association Française pour l'Avancement des Sciences.
- *p.* Bureau des Longitudes.
- A. Bureau International des Poids et Mesures.
- *p.* Commission des Annales des Ponts et Chaussées.
- *p.* Conservatoire des Arts et Métiers.
- *p.* Cosmos (M. L'ABBÉ VALETTE).
- AB. Dépôt de la Marine.
- AB. École des Mines.
- AB. École Normale Supérieure.
- AB. École Polytechnique.
- AB. Faculté des Sciences de la Sorbonne.
- AB. Jardin des Plantes.
- *p.* L'Électricien.

France (continued).
- Paris (continued).
  - A. L'Observatoire.
  - *p.* Revue Scientifique (Mons. H. DE VARIGNY).
  - *p.* Société de Biologie.
  - AB. Société d'Encouragement pour l'Industrie Nationale.
  - AB. Société de Géographie.
  - *p.* Société de Physique.
  - B. Société Entomologique.
  - AB. Société Géologique.
  - *p.* Société Mathématique.
  - *p.* Société Météorologique de France.
- Toulouse.
  - AB. Académie des Sciences.
  - A. Faculté des Sciences.

Germany.
- Berlin.
  - A. Deutsche Chemische Gesellschaft.
  - A. Die Sternwarte.
  - *p.* Gesellschaft für Erdkunde.
  - AB. Königliche Preussische Akademie der Wissenschaften.
  - A. Physikalische Gesellschaft.
- Bonn.
  - AB. Universität.
- Bremen.
  - *p.* Naturwissenschaftlicher Verein.
- Breslau.
  - *p.* Schlesische Gesellschaft für Vaterländische Kultur.
- Brunswick.
  - *p.* Verein für Naturwissenschaft.
- Carlsruhe. See Karlsruhe.
- Charlottenburg.
  - A. Physikalisch-Technische Reichsanstalt.
- Danzig.
  - AB. Naturforschende Gesellschaft.
- Dresden.
  - *p.* Verein für Erdkunde.
- Emden.
  - *p.* Naturforschende Gesellschaft.
- Erlangen.
  - AB. Physikalisch-Medicinische Societät.
- Frankfurt-am-Main.
  - AB. Senckenbergische Naturforschende Gesellschaft.
  - *p.* Zoologische Gesellschaft.
- Frankfurt-am-Oder.
  - *p.* Naturwissenschaftlicher Verein.
- Freiburg-im-Breisgau.
  - AB. Universität.
- Giessen.
  - AB. Grossherzogliche Universität.

Germany (continued).
- Görlitz.
  - *p.* Naturforschende Gesellschaft.
- Göttingen.
  - AB. Königliche Gesellschaft der Wissenschaften.
- Halle.
  - AB. Kaiserliche Leopoldino - Carolinische Deutsche Akademie der Naturforscher.
  - *p.* Naturwissenschaftlicher Verein für Sachsen und Thüringen.
- Hamburg.
  - *p.* Naturhistorisches Museum.
  - AB. Naturwissenschaftlicher Verein.
- Heidelberg.
  - *p.* Naturhistorisch-Medizinischer Verein.
  - AB. Universität.
- Jena.
  - AB. Medicinisch-Naturwissenschaftliche Gesellschaft.
- Karlsruhe.
  - A. Grossherzogliche Sternwarte.
  - *p.* Technische Hochschule.
- Kiel.
  - *p.* Naturwissenschaftlicher Verein für Schleswig-Holstein.
  - A. Sternwarte.
  - AB. Universität.
- Königsberg.
  - AB. Königliche Physikalisch - Ökonomische Gesellschaft.
- Leipsic.
  - *p.* Annalen der Physik und Chemie.
  - AB. Königliche Sächsische Gesellschaft der Wissenschaften.
- Magdeburg.
  - *p.* Naturwissenschaftlicher Verein.
- Marburg.
  - AB. Universität.
- Munich.
  - AB. Königliche Bayerische Akademie der Wissenschaften.
  - *p.* Zeitschrift für Biologie.
- Münster.
  - AB. Königliche Theologische und Philosophische Akademie.
- Potsdam.
  - A. Astrophysikalisches Observatorium.
- Rostock.
  - AB. Universität.
- Strasburg.
  - AB. Universität.
- Tübingen.
  - AB. Universität.

Germany (continued).

Würzburg.

AB. Physikalisch-Medicinische Gesellschaft.

Greece.

Athens.

A. National Observatory.

Holland. (See NETHERLANDS.)

Hungary.

Buda-pest.

p. Königl. Ungarische Geologische Anstalt.

AB. Á Magyar Tudós Társaság. Die Ungarische Akademie der Wissenschaften.

Hermannstadt.

p. Siebenbürgischer Verein für die Naturwissenschaften.

Klausenburg.

AB. Az Erdélyi Muzeum. Das Siebenbürgische Museum.

Schemnitz.

p. K. Ungarische Berg- und Forst-Akademie.

India.

Bombay.

AB. Elphinstone College.

p. Royal Asiatic Society (Bombay Branch).

Calcutta.

AB. Asiatic Society of Bengal.

AB. Geological Museum.

p. Great Trigonometrical Survey of India.

AB. Indian Museum.

p. The Meteorological Reporter to the Government of India.

Madras.

B. Central Museum.

A. Observatory.

Roorkee.

p. Roorkee College.

Ireland.

Armagh.

A. Observatory.

Belfast.

AB. Queen's College.

Cork.

p. Philosophical Society.

AB. Queen's College.

Dublin.

A. Observatory.

AB. National Library of Ireland.

B. Royal College of Surgeons in Ireland.

AB. Royal Dublin Society.

AB. Royal Irish Academy.

Galway.

AB. Queen's College.

Italy.

Acireale.

p. Accademia di Scienze, Lettere ed Arti.

Bologna.

AB. Accademia delle Scienze dell' Istituto.

Catania.

AB. Accademia Gioenia di Scienze Naturali.

Florence.

p. Biblioteca Nazionale Centrale.

AB. Museo Botanico.

p. Reale Istituto di Studi Superiori.

Genoa.

p. Società Ligustica di Scienze Naturali e Geografiche.

Milan.

AB. Reale Istituto Lombardo di Scienze, Lettere ed Arti.

AB. Società Italiana di Scienze Naturali.

Modena.

p. Le Stazioni Sperimentali Agrarie Italiane.

Naples.

p. Società di Naturalisti.

AB. Società Reale, Accademia delle Scienze.

B. Stazione Zoologica (Dr. DOHRN).

Padua.

p. University.

Palermo.

A. Circolo Matematico.

AB. Consiglio di Perfezionamento (Società di Scienze Naturali ed Economiche).

A. Reale Osservatorio.

Pisa.

p. Il Nuovo Cimento.

p. Società Toscana di Scienze Naturali.

Rome.

p. Accademia Pontificia de' Nuovi Lincei.

p. Rassegna delle Scienze Geologiche in Italia.

A. Reale Ufficio Centrale di Meteorologia e di Geodinamica, Collegio Romano.

AB. Reale Accademia dei Lincei.

p. R. Comitato Geologico d' Italia.

A. Specola Vaticana.

AB. Società Italiana delle Scienze.

Siena.

p. Reale Accademia dei Fisiocritici.

Turin.

p. Laboratorio di Fisiologia.

AB. Reale Accademia delle Scienze.

Venice.

p. Ateneo Veneto.

AB. Reale Istituto Veneto di Scienze, Lettere ed Arti.

Japan.
- Tokiô.
  - AB. Imperial University.
  - *p.* Asiatic Society of Japan.

Java.
- Buitenzorg.
  - *p.* Jardin Botanique.

Luxembourg.
- Luxembourg.
  - *p.* Société des Sciences Naturelles.

Malta.
- *p.* Public Library.

Mauritius.
- *p.* Royal Society of Arts and Sciences.

Netherlands.
- Amsterdam.
  - AB. Koninklijke Akademie van Wetenschappen.
  - *p.* K. Zoologisch Genootschap 'Natura Artis Magistra.'
- Delft.
  - *p.* École Polytechnique.
- Haarlem.
  - AB. Hollandsche Maatschappij der Wetenschappen.
  - *p.* Musée Teyler.
- Leyden.
  - AB. University.
- Rotterdam.
  - AB. Bataafsch Genootschap der Proefondervindelijke Wijsbegeerte.
- Utrecht.
  - AB. Provinciaal Genootschap van Kunsten en Wetenschappen.

New Brunswick.
- St. John.
  - *p.* Natural History Society.

New Zealand.
- Wellington.
  - AB. New Zealand Institute.

Norway.
- Bergen.
  - AB. Bergenske Museum.
- Christiania.
  - AB. Kongelige Norske Frederiks Universitet.
- Tromsoe.
  - *p.* Museum.
- Trondhjem.
  - AB. Kongelige Norske Videnskabers Selskab.

Nova Scotia.
- Halifax.
  - *p.* Nova Scotian Institute of Science.
- Windsor.
  - *p.* King's College Library.

Portugal.
- Coimbra.
  - AB. Universidade.
- Lisbon.
  - AB. Academia Real das Sciencias.
  - *p.* Secção dos Trabalhos Geologicos de Portugal
- Oporto.
  - *p.* Annaes de Sciencias Naturaes.

Russia.
- Dorpat.
  - AB. Université.
- Irkutsk.
  - *p.* Société Impériale Russe de Géographie (Section de la Sibérie Orientale).
- Kazan.
  - AB. Imperatorsky Kazansky Universitet.
- Kharkoff.
  - *p.* Section Médicale de la Société des Sciences Expérimentales, Université de Kharkow.
- Kieff.
  - *p.* Société des Naturalistes.
- Moscow.
  - AB. Le Musée Public.
  - B. Société Impériale des Naturalistes.
- Odessa.
  - *p.* Société des Naturalistes de la Nouvelle-Russie.
- Pulkowa.
  - A. Nikolai Haupt-Sternwarte.
- St. Petersburg.
  - AB. Académie Impériale des Sciences.
  - B. Archives des Sciences Biologiques.
  - AB. Comité Géologique.
  - *p.* Compass Observatory.
  - A. Observatoire Physique Central.

Scotland.
- Aberdeen.
  - AB. University.
- Edinburgh.
  - *p.* Geological Society.
  - *p.* Royal College of Physicians (Research Laboratory).
  - *p.* Royal Medical Society.
  - A. Royal Observatory.
  - *p.* Royal Physical Society.
  - *p.* Royal Scottish Society of Arts.
  - AB. Royal Society.
- Glasgow.
  - AB. Mitchell Free Library.
  - *p.* Natural History Society.
  - *p.* Philosophical Society.

Servia.
- Belgrade.
  - *p.* Académie Royale de Serbie.

Sicily. (See Italy.)

Spain.
- Cadiz.
  - A. Instituto y Observatorio de Marina de San Fernando.
- Madrid.
  - *p.* Comisión del Mapa Geológico de España.
  - AB. Real Academia de Ciencias.

Sweden.
- Gottenburg.
  - AB. Kongl. Vetenskaps och Vitterhets Samhälle.
- Lund.
  - AB. Universitet.
- Stockholm.
  - A. Acta Mathematica.
  - AB. Kongliga Svenska Vetenskaps-Akademie.
  - AB. Sveriges Geologiska Undersökning.
- Upsala.
  - AB. Universitet.

Switzerland.
- Basel.
  - *p.* Naturforschende Gesellschaft.
- Bern.
  - AB. Allg. Schweizerische Gesellschaft.
  - *p.* Naturforschende Gesellschaft.
- Geneva.
  - AB. Société de Physique et d'Histoire Naturelle.
  - AB. Institut National Genevois.
- Lausanne.
  - *p.* Société Vaudoise des Sciences Naturelles.
- Neuchâtel.
  - *p.* Société des Sciences Naturelles.
- Zürich.
  - AB. Das Schweizerische Polytechnikum.
  - *p.* Naturforschende Gesellschaft.
  - *p.* Sternwarte.

Tasmania.
- Hobart.
  - *p.* Royal Society of Tasmania.

United States.
- Albany.
  - AB. New York State Library.
- Annapolis.
  - AB. Naval Academy.
- Austin.
  - *p.* Texas Academy of Sciences.
- Baltimore.
  - AB. Johns Hopkins University.
- Berkeley.
  - *p.* University of California.

United States (continued).
- Boston.
  - AB. American Academy of Sciences.
  - B. Boston Society of Natural History.
  - A. Technological Institute.
- Brooklyn.
  - AB. Brooklyn Library.
- Cambridge.
  - AB. Harvard University.
  - B. Museum of Comparative Zoology.
- Chapel Hill (N.C.).
  - *p.* Elisha Mitchell Scientific Society.
- Charleston.
  - *p.* Elliott Society of Science and Art of South Carolina.
- Chicago.
  - AB. Academy of Sciences.
  - *p.* Field Columbian Museum.
  - *p.* Journal of Comparative Neurology.
- Davenport (Iowa).
  - *p.* Academy of Natural Sciences.
- Ithaca (N.Y.).
  - *p.* Physical Review (Cornell University).
- Madison.
  - *p.* Wisconsin Academy of Sciences.
- Mount Hamilton (California).
  - A. Lick Observatory.
- New Haven (Conn.).
  - AB. American Journal of Science.
  - AB. Connecticut Academy of Arts and Sciences.
- New York.
  - *p.* American Geographical Society.
  - *p.* American Museum of Natural History.
  - *p.* New York Academy of Sciences.
  - *p.* New York Medical Journal.
  - *p.* School of Mines, Columbia College.
- Philadelphia.
  - AB. Academy of Natural Sciences.
  - AB. American Philosophical Society.
  - *p.* Franklin Institute.
  - *p.* Wagner Free Institute of Science.
- Rochester (N.Y.).
  - *p.* Academy of Science.
- St. Louis.
  - *p.* Academy of Science.
- Salem (Mass.).
  - *p.* American Association for the Advancement of Science.
  - AB. Essex Institute.
- San Francisco.
  - AB. California Academy of Sciences.

United States (continued).

Washington.

- AB. Patent Office.
- AB. Smithsonian Institution.
- AB. United States Coast Survey.
- B. United States Commission of Fish and Fisheries.
- AB. United States Geological Survey.

United States (continued).

Washington (continued).

- AB. United States Naval Observatory.
- *p*. United States Department of Agriculture.
- A. United States Department of Agriculture (Weather Bureau).

West Point (N.Y.)

- AB. United States Military Academy.

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I. CROONIAN LECTURE.—*Observations on Isolated Nerve* (*with particular reference to Carbon Dioxide*).

By AUGUSTUS D. WALLER, *M.D.*, *F.R.S.*

Received—Chapters I. and II., December 10, 1895; Chapter III., January 16, 1896; Chapter IV., May 28, 1896. Lecture delivered, March 12, 1896.

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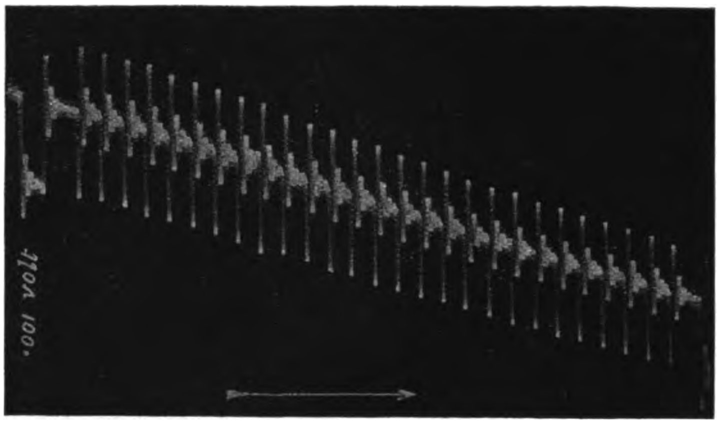
CHAPTER I.—INTRODUCTION.

As was pointed out ten years ago by **WEDENSKI**, from telephone observations of the negative variation, by **WALLER**, from galvanometric observations of the same, and by

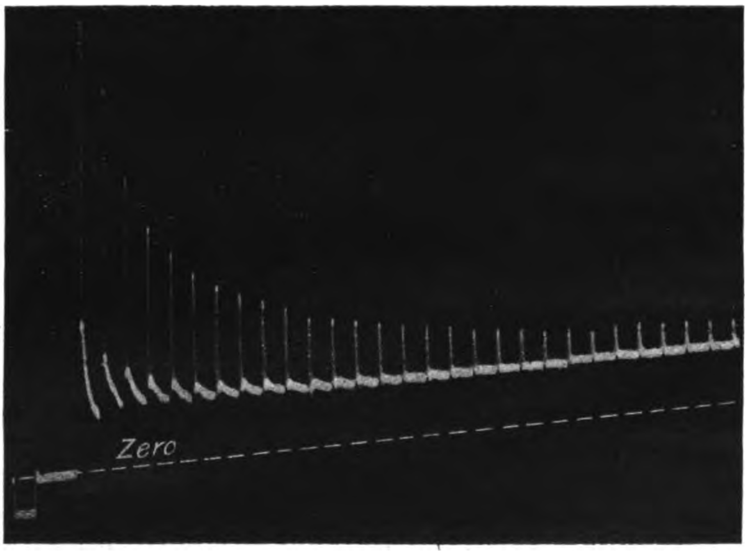
Bowditch from the observation of long-persisting excitability in the nerves of temporarily curarised mammals, nerve is now admitted to be practically inexhaustible. The apparent exhaustion of nerve when a nerve-muscle preparation is submitted to prolonged excitation is, as was first demonstrated in Bernstein's experiment, not an exhaustion of nerve, but an exhaustion of the organ of intermediation between nerve

Fig. 1. (Obs. 334.



Normal series of negative variations of current of injury of nerve. Excitation each minute for ⅛ minute. The general decline south signifies a declining current of injury. Each negative deflection consists of a southward swing, followed by instrumental oscillations above and below the position of rest of the suspended magnets of a Thomson galvanometer. The deflection at the beginning of the series is by 0·001 volt.

Fig. 2. (Obs. 1501.)



Series of negative variations of current of injury of muscle, to show the contrast between their rapid decline and the undiminishing, or slightly diminishing, series of negative variations of nerve. Maximal indirect tetanisation for 7·5 seconds, at intervals of 1 minute. The deflection at commencement of record is by 0·001 volt. The rise of the base line is accidental. Dead-beat galvanometer.

and muscle, which, as pointed out by WALLER, is the weak link in the neuro-muscular chain, being the point at which functional failure is first manifested, in fatigue, in nerve degeneration, in intoxication by curare (BERNARD), and at death.

Taking as the sign of action artificially excited in a nerve, the negative variation of its current of rest (DU BOIS-REYMOND) or current of injury (HERMANN), the long endurance by nerve of excitation excessive in strength and in length, is well shown by prolonged photographic records of the galvanometric indications, which exhibit little or no decline, in marked contrast with similar records of the negative variation of muscle which declines *pari passu* with the declining contraction due to fatigue of the motor end plates. This steady regularity of response renders nerve pre-eminently suitable to the systematic study of its experimental disturbance.

§ 1. *Method.*

The excised sciatic nerve of the frog is laid across two pairs of electrodes enclosed in a moist chamber through which gases can be passed; a tetanising current, of uniform duration and strength, excites the nerve once a minute through one pair of electrodes (of platinum, or unpolarisable); from the other pair of electrodes (unpolarisable) the nerve current and its negative variation at each minute are led off to a galvanometer.*

The tetanising current (lasting for $\frac{1}{8}$ minute) is effected by a revolving key in the primary circuit of a Berne standard induction coil; a reverser in circuit enables the direction of exciting currents to be reversed; these are "unmodified," *i.e.*, with the break shocks alone effective; two Leclanché cells (MUIRHEAD'S pattern) supply the primary coil; a short-circuiting key in this circuit is connected with a separate galvanometer, so that the current strength may be verified as constant; the secondary coil is fixed at a distance of 38 centims. from the primary, affording about 10 units of the Berne scale.

The nerve and galvanometer circuit, controlled by two short-circuiting keys (fig. 3, K_1 and K_3), connected with the nerve and galvanometer circuit respectively, could by a third key (K_2) be put in connection with a standard E.M.F. of $\frac{1}{1000}$ volt. A fourth key (K_4) is connected with a demonstrating galvanometer, the readings of which are observed on a screen in the usual way.

The moist or gas-chamber, with three sides of ebonite and three sides of glass, had a capacity of 30 cub. centims. The interval between the centres of the leading-off electrodes was 10 millims., that between the exciting electrodes was 3 millims., and that between the exciting and leading-off electrodes was 15 millims.

The galvanometer spot (image of a vertical slit in front of a paraffin lamp) fell upon a horizontal slit in a vertical box in which an "ordinary" photographic quarter plate was let down by clockwork.

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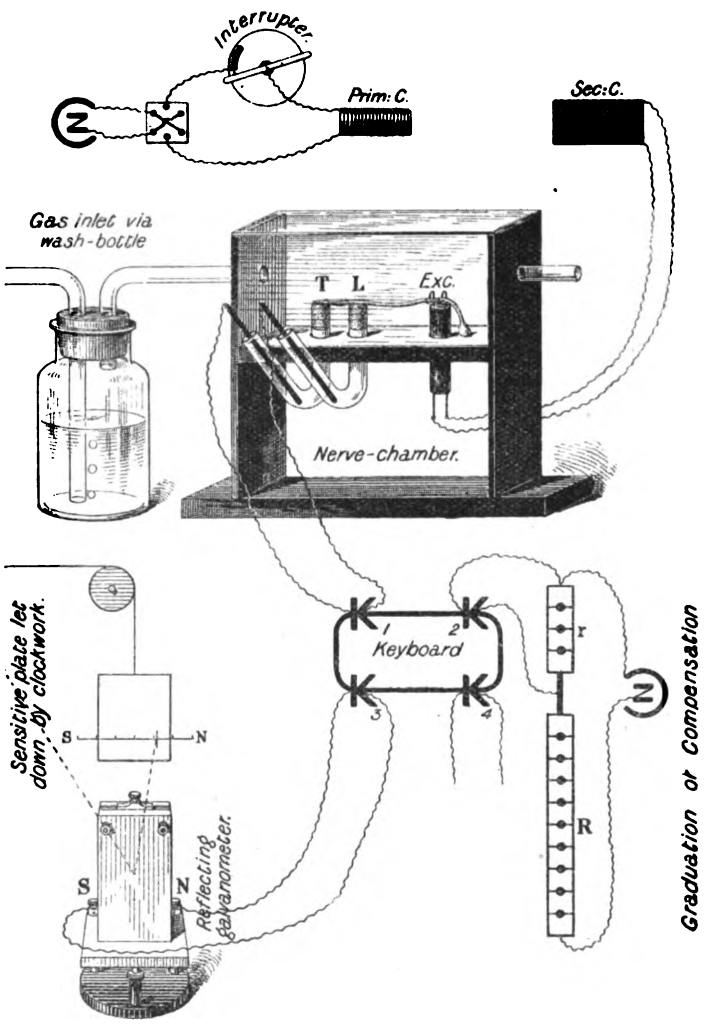
* *Vide* note to Table D, p. 66. All the earlier records (*e.g.*, fig. 1) were taken with the partially-damped instrument; many of the later records (*e.g.*, figs. 66, 67, 68 and figs. 49 to 56) were taken with a dead-beat instrument.

Fig. 3.


Interrupter
Prim: C.
Sec: C.
Gas inlet via wash-bottle
T
L
Exc.
Nerve-chamber.
Sensitive plate let down by clockwork.
S
N
1
2
Keyboard
3
4
r
R
S
N
Reflecting galvanometer.
Graduation or Compensation

Plan of Apparatus.

The *nerve-chamber* contains the nerve resting upon a pair of unpolarisable electrodes connected with K_1, and a pair of platinum electrodes, through which the nerve is excited. The wash-bottle serves to prevent drying of the nerve, and, in certain cases, is used to stop acid vapour.

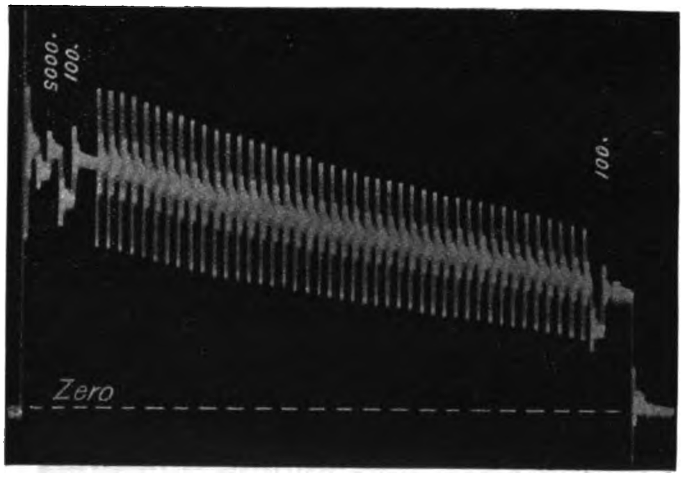
The *exciting apparatus* is represented above; the circular interrupter in the primary circuit revolves once a minute, and makes contact at a mercury pool for $\frac{1}{8}$ of each revolution. The vibrating interrupter of the coil starts as the circuit is completed, and the nerve is thus tetanised each minute for $7\frac{1}{2}$ seconds, at a frequency of 70–75 interruptions per second.

The *keyboard* is composed of four bridging keys: K_1 in connection with the nerve at T and L, K_2 with the compensator, K_3 with the recording galvanometer, and K_4 on occasion with a demonstrating galvanometer. When all the keys are closed, everything is short-circuited through them; the key-board is then simply a metallic ring. Opening K_1 and K_3 puts the nerve into connection with the galvanometer; opening K_2 lets into the nerve-circuit any suitable fraction of a volt from the cell and rheostats *r*.R. To take 0·001 volt from a Leclanché cell, *r* is taken = 10 ohms, and R = 14,690 ohms; to take a polarisation current of 0·01 volt, *r* is taken = 100 ohms, and R = 14,600 ohms, &c.

The connections in the diagram are represented such that the current of injury passes from left to right in the nerve, and in the galvanometer, viz., from T to L and from S to N, reading upwards in the final record. The compensation or graduation current reads downwards. A negative variation reads downwards. A positive variation reads upwards.

The order of procedure in experiment was as follows:—The nerve was dissected out, cut near the knee joint, and left in connection with a piece of spinal column to serve as a handle. It was then laid across the two pairs of electrodes and tested by a tetanising current, as above. Electrotonic effects were tested for by reversal of the exciting current, and by crushing the nerve in the interpolar region; unipolar effects by removing one wire; magnetic effects by removing both wires of the secondary coil; escape of primary current was also tested for and excluded by careful insulation. The excitatory deflection was, if necessary, reduced by shunting the galvanometer. The record was then started, a standard deflection by $\frac{1}{1000}$ volt being first taken through the nerve and galvanometer, shunted or not, to serve as a term of comparison, and as a witness to any possible alterations of resistance that might have occurred during experiment. This standard deflection was repeated whenever it seemed advisable by closure of the appropriate key. A sufficient number of "normal" excitatory deflections having been recorded, usually 10 to 15, the experimental gas was passed through the gas-chamber, the time of passage of the gas being signalled by the light of a candle, about 10 feet distant, turned upon the slit behind which the sensitive plate was descending. In general the duration of an experiment was 1 hour, exceptionally ½ hour, or 2 or 4 hours.

Fig. 4. (Obs. 309.)

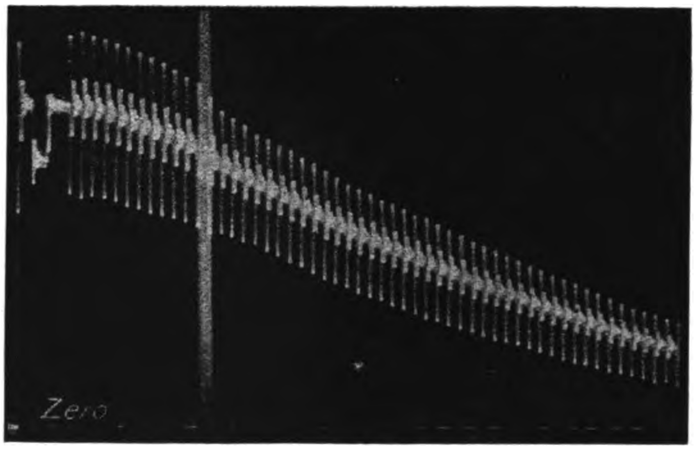


Similar series to that of fig. 1, on a more slowly moving recording surface. The zero line of the galvanometer is indicated; the standard deflections at beginning and end of the record are by $\frac{1}{1000}$ volt.

In earlier observations, while the first sciatic was under experiment, the second sciatic was left undisturbed in the animal and then prepared for the second experiment. In later observations both nerves were removed at the same time and kept in normal saline until required. (Compare figs. 5 and 6.)

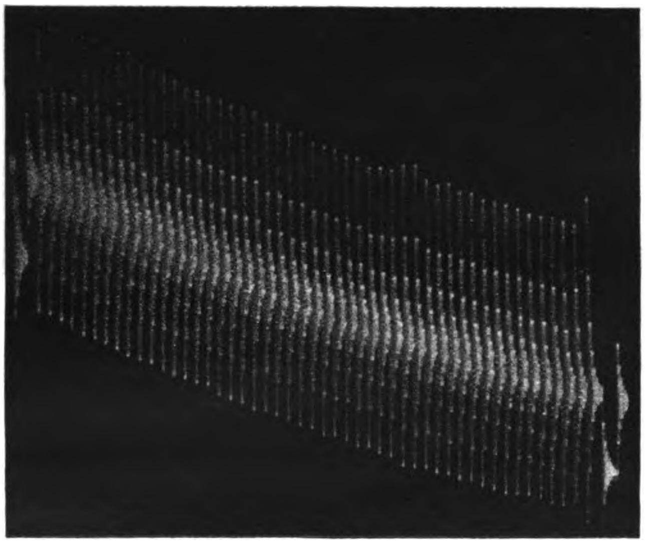
In order to secure the uniformity and easy legibility of record, the disposition of

Fig. 5.. (Obs. 336.)



Similar series. Negative variation declining more rapidly than usual. Nerve left for about an hour in the pithed frog before use. The vertical white bar marks where nitrous oxide was passed into the nerve-chambers.

Fig. 6. (Obs. 708.)



Similar series. Negative variation of nearly constant magnitude. The excised nerve had been kept for 18 hours in physiological saline. The difference in the decline of the negative variation in this and in preceding figure is probably due to the action of CO_2 in the case of fig. 5, and the absence of such action in the case of fig. 6. The positive after-effect is well marked, giving an upward excursion of the magnet considerably in excess of the instrumental oscillation. (See pp. 66 and 84.)

connections adopted (transverse section of nerve to north terminal of galvanometer, longitudinal surface to south terminal) was such as to give:

NORTHWARD OR POSITIVE DEFLECTION BY THE NORMAL CURRENT OF INJURY.

SOUTHWARD OR NEGATIVE DEFLECTION BY THE NORMAL CURRENT OF ACTION.

And, for the same reason, the standard deflection by $\frac{1}{1000}$ volt was always taken in one direction, viz, southward.

The records read from right to left, north and south being their upper and lower borders respectively; positive deflections read upwards, negative deflections downwards.

With a fresh nerve, apparatus and connections disposed as above, the current of injury (north or above the zero line) gradually and steadily decreases (southwards or downwards), this decrease, according to ENGELMANN'S* observations and interpretation, is due to a diminishing negativity at and near the transverse section of the nerve; the negativity having fallen, may be raised again to or nearly to its original magnitude by a fresh transverse section; the original current and its decline are thus shown to be due to chemical action near the dying cut end rather than at the intact longitudinal surface. The line of decline during an hour's observation may be straight or concave to the abscissa, or convex at first, then concave to the abscissa.

The series of negative deflections (first swing south, followed in the case of the imperfectly damped galvanometer, by oscillations of the magnet north and south of the position of rest) frequently exhibits a progressive diminution, which one is at first thought inclined to regard as causally associated with the decline of the current of injury. Some such association may indeed obtain, but on a considerable number of observations is by no means clear or prominent, for with a large current of injury the negative deflection is sometimes small, and with a small current of injury it is sometimes large.

The progressive diminution of the current of injury might be significant of fatigue by the repeated excitations, or it might be due to a variety of accidental causes such as an unusually rapid death of a nerve, or a contamination of the clay electrodes by sulphate of zinc, or to acidity of the clay or of the salt solution. All these accidental causes excluded, it is easily seen that declining magnitude of the negative variation is not a fatigue effect, inasmuch as it proceeds uninfluenced by prolonged intermission of the excitation. Later experiments, as will be described below in detail, showed that one most effective cause of the decline was the previous action of carbon dioxide; and by yet other experiments it was rendered at least highly probable that another effective cause was the development of an opposite after-effect at and near the longitudinal lead-off.

In the earlier observations, the duration of which was, as a rule, limited to 1 or 2 hours, an effect was noticed which was then regarded as somewhat exceptional (see figs. 7 and 8), but which in later observations, the duration of which has been often extended over several hours, has been recognised to be of frequent occurrence, viz., a reversal of the negative variation (south), and its replacement by a positive variation (north); the latter is shown to be a true physiological effect by the usual tests, by its susceptibility to anæsthetic vapours and to carbon dioxide; by the last-named gas in particular such a positive variation is promptly and temporarily abolished. It was found not to be in any constant association with a reversed current of injury, which, indeed, was a quite exceptional phenomenon, due probably to some accidental injury at the longitudinal lead-off; the dying nerve at this point was then presumably negative to more nearly dead nerve on the side of the transverse lead-off.

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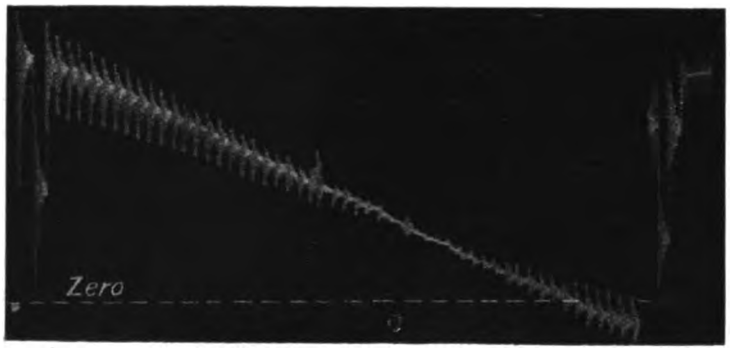
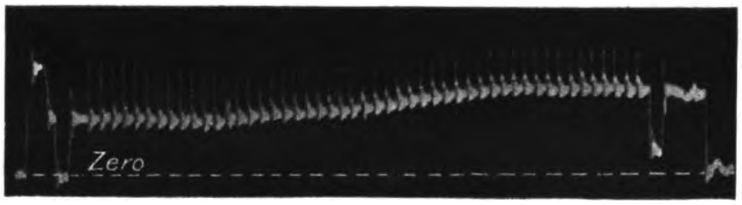
* ENGELMANN. "Untersuchungen zur Lehre von der Muskel- und Nerven-elektricität," 'PFLÜGER'S Archiv,' vol. 15, 1877, p. 116.

Fig. 7. (Obs. 279.)



Gradual reversal of the "normal" (south or negative) deflection, and appearance of a reversed (north or positive) deflection.

Fig. 8. (Obs. 842.)



Reversed or positive variation.

The nerve had been kept in physiological saline for 8½ hours after removal, and had been used the hour previously for an experiment with CO_2.

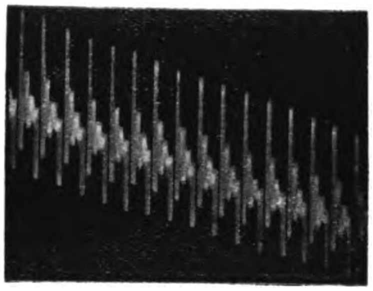
When first observed the variation was composed of a small negative deflection followed by a large positive after-deflection. The variation in the figure is composed of a positive deflection (during excitation) followed by a second positive deflection (at the end of excitation).

The period of the magnet is 15 seconds; the relation of its first swing from the position of rest to its first swing-back beyond that position is $\frac{+36}{-17}$. The duration of excitation is 7½ seconds.

A reversed variation, positive or northward in place of negative or southward, is difficult to explain, and any explanation is bound to be more or less hypothetical.

Several possibilities present themselves: (1) the reversal of excitatory deflection may be due to a reversal of action (or of greater action) in the parts of the nerve at and near the two leading-off electrodes; the normal south deflection depends upon action predominant at and near the longitudinal lead-off, the reversed north deflection might depend upon action becoming predominant at the transverse lead-off in consequence of some accidental and progressive injury near the longitudinal lead-off. Or the reversal might be (2) a phenomenon of the same order as HERING'S* "positive Nachschwankung." Or (3) the phenomenon and its reversal might be of an electrotonic nature. For reasons that will be given later, the second appears to me as the more probable explanation.

Fig. 9. (Obs. 102.)



Portion of a series to show state of nerve intermediate between the first state (predominant south or negative excitatory deflection), and the third state (predominant north or positive excitatory deflection), viz., in which a small negative effect is followed by a larger positive after-effect.

The oscillation decrement in conjunction with the duration of excitation is such that a normal swing-back is equal to two-thirds of the original swing. In this case, therefore, a negative deflection of 7·5 has a positive oscillation of 5 millims., and the net positive after-effect is obtained by subtracting this value from the recorded after-effect, *i.e.*, by subtracting 5 from 12.

In the great majority of my experiments the negative deflection was normal, viz., a southward swing followed by a smaller northward swing-back in accordance with the oscillation decrement of the suspended magnet. But in a considerable minority of instances occurred what is, perhaps, hardly to be characterised as exceptional or abnormal, viz., the back-swing (north) was greater than the original (south) deflection (see fig. 9), and, in some cases, the original south deflection was small and sluggish and cut short by a sharp large deflection north. Instrumental fallacy was to the best of my knowledge excluded; moreover records occurred where, under the influence of carbonic acid and of ether, the relations between south and north variations were gradually and temporarily changed in a way that could only be due to alterations developing in the nerve itself, and, finally, in some cases, most frequently in stale nerves and in drugged nerves (by urea, *e.g.*), the excitatory variation was throughout reversed (see fig. 8).

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* HERING, "Ueber positive Nachschwankung des Nervenstromes nach electrischer Reizung," 'Wiener Sitzungsberichte,' vol. 89, 1884, p. 219; HEAD, "Ueber die negativen und positiven Schwankungen des Nervenstromes,' 'PFLÜGER'S Archiv,' vol. 40, 1887, p. 207.

§ 2. *Concerning the Unfatiguability of Nerve. Relation between the Magnitude of Stimulation and the Magnitude of Electrical Effect.*

Two characteristics of the nerve-response should be mentioned at this stage, as being probably significant of a relative simplicity of this form of excitable matter, a simplicity that may be regarded as rendering nerve the most favourable among living tissues for the study of modifications by chemical reagents. These are :—

(1). The fact that in nerve the relation between magnitude of stimulus and magnitude of electrical effect is arithmetical within at least a considerable range, exceeding what, judged by the muscular response, may be termed the "physiological" range.*

(2). The fact just alluded to that the electrical effect increases with increasing magnitude of stimulus much beyond the physiological maximum effect as gauged by muscle.

Both these points have been reported upon elsewhere† and are alluded to here only inasmuch as they were at the outset of these experiments taken to be indicative of the relative simplicity of nerve-protoplasm, and having regard to the considerable range within which the electrical effects had been found capable of plus and minus variations (*e.g.*, between 2 and 20 or more stimulation units, as compared with a physiological range between 2 and 5 units), a stimulation strength of 10 units was uniformly made use of throughout these experiments.

Whether the adoption of this medium stimulation strength was essential or no, has not been fully determined; such preliminary experiments as were made, indicated weak stimuli as best adapted to the demonstration of increased electro-mobility, and strong stimuli to that of diminished electro-mobility. A medium strength was therefore adopted as a constant condition of experiment, at least throughout the first 800 observations; different strengths were used subsequently, and in some cases the stimulation strength for long series was selected three times the minimal value. Alterations of the direction of the deflection, with alterations of current strength, will be considered at a future stage.

No regard has been paid in these observations to a distinction between direct and indirect excitability, between the excitability at the point of stimulation, and the excitability aroused by propagation along the nerve ("conductivity").

---

* This may be regarded as harmonising with the view that electrical excitation is due to electrolytic polarisation. I find, also, that HERMANN'S "polarisation increment" increases arithmetically with increasing strength of the polarising current.

† 'Proc. Physiol. Soc.,' 1895, p. 35. 'Brain,' 1895, p. 200. The second of the two points mentioned has previously been noticed by HERMANN ('PFLÜGER'S Archiv,' VII., 1873, p. 327).

Preliminary experiments were indeed made in order to test whether modifications

Fig. 10. (Obs. 101.)

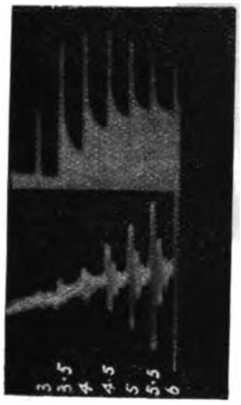


Fig. 11. (Obs. 134.)

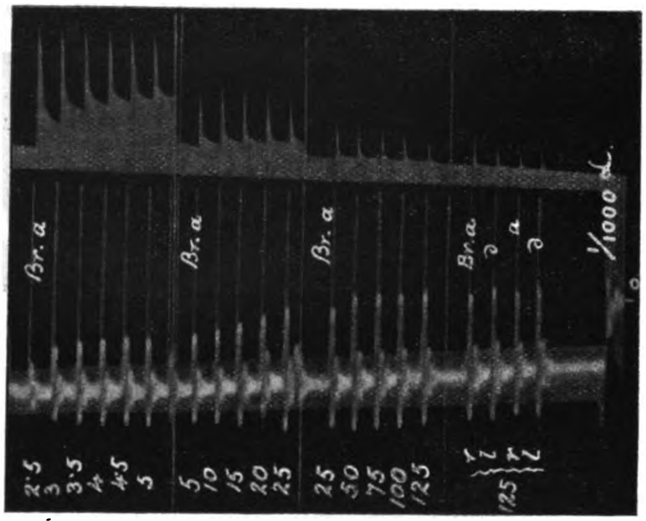


Fig. 10. Simultaneous record of the negative variation of nerve and of the contraction of muscle with increasing strength of stimulation (2·5 to 125 units of Berne coil).

The muscular response is dying off during the experiment, by lapse of time and by fatigue. The nerve response is kept up at a normal level, and increases in magnitude with increasing strength of stimulation (2·5 to 5 units of Berne coil).

The muscular response is dying off during the experiment, by lapse of time and by fatigue. The nerve response is kept up at a normal level, and increases in magnitude with increasing strength of stimulation, from 2·5 to 5, from 5 to 25, and more slowly up to about 50 units; at 125 units tests are made with reversal of direction of exciting currents, their inequality indicates that at this strength unipolar or electrotonic effects may become sensible; at lower strengths reversal of the exciting current was of no effect upon the magnitude of deflection; at the lowest, viz., minimal strengths differences were obtained in the nerve as well as in the muscular response signifying differences in excitation according to its direction (break currents).

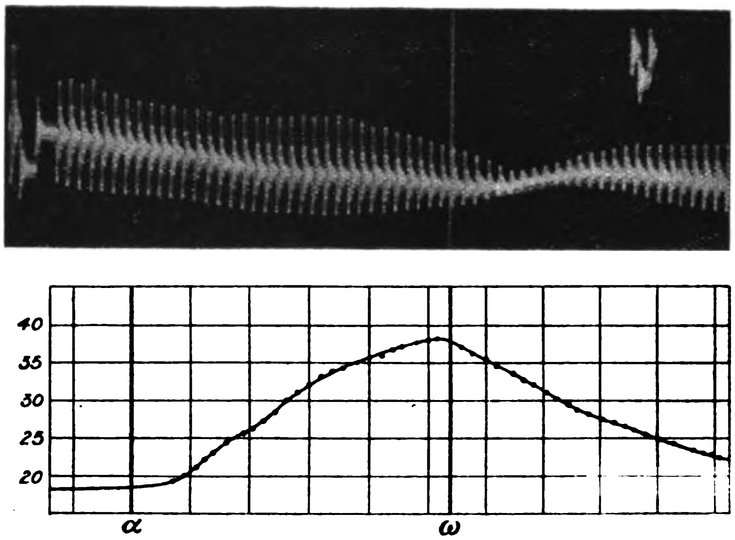
N.B.—In figs. 10 and 11 the current of injury was downwards or south, and falls upwards or north; the negative variation was upwards.

Fig. 11. Simultaneous record of the negative variation of nerve and of the contraction of muscle with increasing strength of stimulation (3 to 6 units of Berne coil).

The effect in nerve increases arithmetically with the stimulation, and continues to increase with increasing strength of stimulation beyond the point at which maximum tetanus of muscle is produced. The maximum contraction grows less in the progress of experiment.

by reagents were at the leading-in (stimulating) electrodes, or at the leading-out (galvanometer) electrodes. These experiments will be described in connection with anæsthetics. At present, it will be sufficient to state that the modifications of excitability (or of "electro-mobility"), were modifications principally at the leading-out electrodes, by which the entire nerve was, so to say, "sampled." Other preliminary experiments were made (see fig. 23) to determine whether such propagated effects behaved in any way differently from directly excited effects; the two circuits (exciting and galvanometer) were conjoined so that the nerve, secondary coil, and galvanometer formed one circuit, with the unpolarisable electrodes serving as leading-in and leading-out electrodes. The nerve was then excited with alternating currents (make and break) weak enough not to disturb the galvanometer, yet strong enough to disturb the nerve (viz., five stimulation units), first in one, then in the opposite direction, and the negative variation by direct excitation was

Fig. 12. (Obs. 773.)



Effect of a rise of temperature from 18° to 38° upon the nerve response. The delay between the maximum temperature reading and the maximum diminution of the nerve response is probably owing to the "lag" of the apparatus between the nerve and the source of heat. The nerve was in a glass chamber in a copper oven, under which a small spirit-lamp flame was placed at *α* and removed at *ω*. The temperature chart below is that of corresponding readings each minute of a thermometer in the oven. No marked effect occurs with a rise of at least 10°; with a rise to 38°—viz., of 20°—the response diminishes; with the subsequent fall of temperature the response increases again.

The record is given in illustration of the fact that the response of fresh nerve is not affected by slight variations of temperature. The effects of considerable variations, as regards the character and sign of the response, will be described and considered in connection with the detailed study of positive and negative effects of excitation.

N.B.—The actual magnitudes of excursions, *e.g.*, in fig. 13, as compared with fig. 12, are of no account as indicative of magnitudes of nerve-effects in terms of potential. The resistance differs in different nerves, and the galvanometer is more or less shunted. The magnitudes of excursions must in all cases be compared with the magnitude of the standard excursion by 0·001 volt taken at beginning and end of each observation.

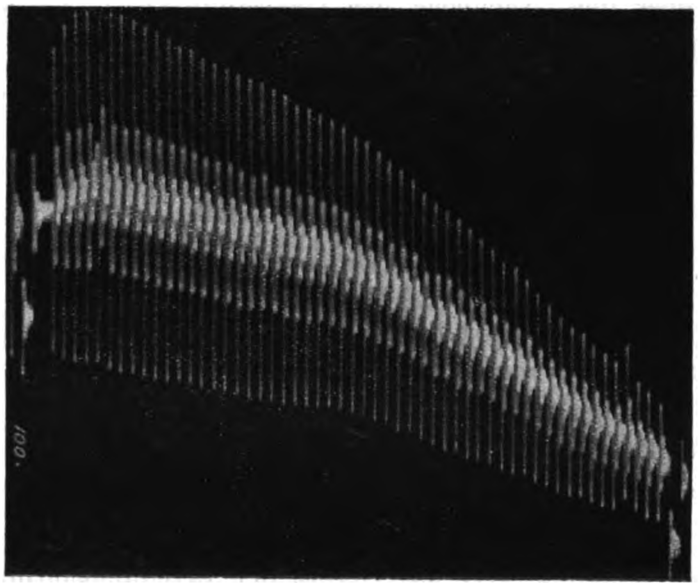
compared and found to be identical with the negative variation by propagated excitation. This conjoint method might, indeed, have been systematically followed, but for several reasons it was preferred to apply stimulation to a separate part of the nerve, regarding the latter simply as a strand of excitable protoplasm to be disturbed at one point, the disturbance being measured at another point, under a variety of chemical conditions.

§ 3. *Temperature, Moisture, and Atmospheric Pressure.*

Preliminary observations were made as to the influence of temperature and moisture—of the former by enclosing the gas-chamber in an oven of which the temperature was gradually raised and lowered, of the latter by leaving the gas-chamber open with the nerve and electrodes exposed to the air.

As regards temperature, it was found that between 30° and 40° the excitability declined and disappeared, to return, however, with subsequent fall of temperature (fig. 12).

Fig. 13. (Obs. 825.)



Effect of drying by evaporation upon the response of nerve. Stimulation as usual, 10 units tetanisation for $\frac{1}{8}$ minute at each minute.

Nerve kept in physiological saline for $2\frac{1}{2}$ hours after excision; lid of gas-chamber removed. In the absence of evaporation such a nerve would probably have given an uniform series, as in fig. 6. The relative magnitudes of the deflections by 0·001 volt at beginning and end of the series indicate to what extent the diminishing deflection is due to increasing resistance of the nerve.

As regards moisture, it was found that the excitability of a drying nerve progressively diminishes (fig. 13), being restored, however, by subsequent moisture.

The possible influence of alterations of barometric pressure was also examined on nerves in nerve-chambers, within an iron vessel, in which the pressure was raised to 3 atmospheres and depressed to ⅓ atmosphere. The results of these alterations were throughout negative.

It was therefore concluded that small changes of temperature, of moisture and of pressure, such as may occur in the gas-chamber, are negligible.

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" "The Quantitative Relation between Stimulation and Negative Variation of Nerve." 'Proc. Physiol. Soc.,' June, 1895.

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CHAPTER II.—THE INFLUENCE OF CARBON DIOXIDE.

§ 1. *Action of "much"* CO_2 *and of "little"* CO_2 *on Normal Nerve.*

Reagents in the state of gas or vapour are obviously the most convenient means of testing chemical modification of nerve according to the method described in the previous chapter, inasmuch as the nerve remains undisturbed throughout observation.

Chloroform, ether, and other anæsthetics were first tested, with results such as might be anticipated from their known action on man and animals. These were demonstrated at the November meeting of the Physiological Society, and will be fully reported upon in a future communication.

Carbon dioxide, carbon monoxide, nitrous oxide, oxygen, methane, coal gas, hydrogen, hydrogen sulphide, chlorine, ammonia, hydrocyanic acid, amyl nitrite (impure) were next tested, with results partly expected, partly unexpected. Thus, *e.g.*, coal gas, oxygen, carbon monoxide, and nitrous oxide produced no effect, while more or less pronounced effects were obtained from all the other gases named.

Among these various gases carbon dioxide afforded results of most physiological interest, as, indeed, might have been expected in the case of one of the chief terminal products of protoplasmic action.

Detailed study of the action of CO_2, in varying amounts and under various conditions, afford results of great simplicity and experimental certainty, serving as a foundation upon which rest: 1. Experimental evidence of a production of CO_2 by active nerve. 2. Experimental separation of two opposed movements (of assimilation and dissimilation, or of polarisation and depolarisation ?) in nerve, oppositely influenced under certain conditions: (*a*) by CO_2 from outside, (*b*) by CO_2 produced within nerve itself.

These two subjects cannot, however, be discussed with any advantage until the action of CO_2 upon isolated nerve has been fully ascertained and considered; this is the more necessary in that its effects are not at all what might have been anticipated from the frequently quoted experiment of GRÜNHAGEN* concerning the action of CO_2 upon the nervous conductivity.

The characteristic action of CO_2 upon normal (or nearly normal) isolated nerve will be best and most briefly presented by the following summary notes of fifty consecutive† galvanographic records, together with a few selected representative records, and followed by the conclusions to be drawn from these fifty observations.

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* GRÜNHAGEN, "Versuche über intermittirende Nervenreizung," 'PFLÜGER'S Archiv,' vol. 6, 1872, p. 180.

† SZPILMAN and LUCHSINGER ('PFLÜGER'S Archiv,' vol. 24, 1881), extended GRÜNHAGEN'S experiment and contradict his conclusion.

TABLE A.—Summary of Observations on the Action of Carbon Dioxide upon Normal Nerve.

No.	Plate No.	Duration of CO_2 current.	Negative variation.	Remarks.
1	172	12 minutes	*Before:* 15 millims. . . . *During:* augmentation to 20, giving way to diminution to 5 *After:* augmentation to 70, gradually declining	$\frac{1}{1000}$ volt gave a deflection of 25 millims.
2	173	2 "	*Before:* 15 millims. . . . *During:* 25 " *After:* 50 "	Same nerve.
3	182	8 "	*During:* abolition . . . . *After:* augmentation	Base-line rises north.
4		4 "	*During:* abolition . . . . *After:* augmentation	25 minutes' interval between first and second trials.
5	183	3 "	Slight after-augmentation .	On a previously fully etherised nerve.
6	190	3 "	Ditto	On a previously chloroformed nerve.
7	194	4 "	*Before:* 20 millims. . . . *During:* 0 " *After:* 60 "	Base-line rises north after passage of CO_2.
8	195	3 "	*During:* abolition . . . . *After:* augmentation	7 minutes between the two trials.
		3 "	Ditto	
9	196	2 "	Ditto	Same nerve.
10	198	2 "	Ditto	Base-line falls during, rises after.
11	200 (fig. 14)	2 "	Ditto	Typical effect, viz., primary abolition, secondary augmentation.
12	240	2 "	No effect	Nerve of a naturally dead frog.
13	245	1 "	Expired air: augmentation	Presumably a CO_2 effect.
		1 "	Room air: no effect	
		1 "	Expired air: augmentation	
		1 "	Room air: no effect	
14	413	3 "	*Before:* 4 millims. . . . *During:* 0 " *After:* 30 "	30 minutes after CO_2 the original S. deflection gave way to N.
15	416	1 "	Similar to No. 1	After $CaBr_2$.
16	432	1 "	Typical effect	After $\left\{\begin{array}{l}CHCl_2.\\CH_2Cl.\end{array}\right.$
17	437	1 "	Ditto	Ditto.
18	464	1 "	Diminution followed by augmentation	After recovery from ether depression.
19	521	1 "	Ditto	
		1 "	Ditto	
20	522	10 "	Augmentation for 2 minutes, giving way to abolition for 10 minutes, followed by augmentation *Before:* 15 millims *During:* 20 . . . . 0 *After:* 60 . . . . declining	
21	537 (fig. 15)	5 "	Primary augmentation, diminishing, followed by secondary greater augmentation	The negative S. effect is relatively larger, the positive N. after-effect is relatively smaller after the passage of CO_2.

TABLE A.—Summary of Observations on the Action of Carbon Dioxide upon Normal Nerve—(continued).

No.	Plate No.	Duration of CO_2 current.	Negative variation.	Remarks.
22	561	2 minutes	Primary diminution, secondary augmentation	After recovery from ether. The normal S. gradually gave way to an N.S. deflection.
23	574	1 ,,	No effect	After ammoniated chloroform. No recovery. Twice tested.
24	579	1 ,,	Typical effect	
25	598 (fig. 20)	Expired air 2 minutes	Primary augmentation . .	To test the effect of expired air; 3 per cent. CO_2.
26	599	1 ,,	Abolition followed by slow recovery. No augmentation within 30 minutes	The original deflection was N.; after CO_2 it became N.S.N., gradually giving place to N. The plate was twice used, and cannot therefore be precisely read. A variation of similar character N.S.N. is recorded on Plate 758.
27	607	1 ,,	Typical effect	
28	610	1 ,,	Ditto	
29	627	13 ,,	Ditto	
30	633 (fig. 17)	2½ ,,	Ditto	
31	638	2 ,,	Ditto	
32	641	2½ ,,	Ditto	
33	646	1 ,,	Abolition followed by recovery; no subsequent augmentation	Nerve of a frog killed some hours previously; left *in situ*, *i.e.*, subject to the reducing action of the tissues.
34	647	3 ,,	Primary augmentation followed by secondary greater augmentation	CO_2 in very slow stream. At about the 5th minute after CO_2, it was noticed that the S. effect was augmented while the N. after-effect was diminished; later both were increased.
35	648	3 ,,	Primary diminution, secondary augmentation	After imperfect recovery from ether.
36	650		Slight primary augmentation, giving way to diminution, followed by secondary augmentation	Double gas-chamber. CO_2 passed through upper or excitation compartment. Greater augmentation of S. than of N.
37	651	3 ,,	Primary augmentation, giving way to diminution, followed by secondary augmentation	Double gas-chamber same nerve. CO_2 through lower or lead-off compartment. Effects similar to but more pronounced than those of previous experiment.
38	652 (fig. 18)	1 ,,	Primary augmentation, diminishing slightly, followed by secondary augmentation	Double gas-chamber. CO_2 through lead-off half. Augmented S. with diminished N.
39	653	1 ,,	Slight diminution, followed by slight augmentation	Double gas-chamber. Same nerve. CO_2 through leading-out half.
40	654	100 cub. centims. 100 ,, ,,	Slight augmentation . . . Ditto	Base-line rises. Ditto.

TABLE A.—Summary of Observations on the Action of Carbon Dioxide upon Normal Nerve—(continued).

No.	Plate No.	Duration of CO_2 current.	Negative variation.	Remarks.
41	671 (fig. 21)	. . . . . .	. . . .	To test a presumable CO_2 effect in a nerve left subject to the action of surrounding tissues. Frog killed 18 hours previously. The negative deflection is very large (= about 0·004 volt) as compared with the usual normal (= about 0·001 volt) and declines very rapidly.
42	672 (fig. 22)	. . . . .	Diminution followed by imperfect recovery	Second nerve of same frog. Imperfect CO_2 effect upon the presumably already carbonised nerve.
43	673	1 minute	Ditto	Same nerve.
44	674 (fig. 19)	1 ,,	Slight primary augmentation, declining, followed by large secondary augmentation	A perfectly fresh nerve, original deflection = 0·0013, after CO^2 = 0·0035, the S effect is greater, while the N after-effect is still smaller.
45	740	4 ,,	Abolition followed by small augmentation	Frog killed 2 hours, nerve *in situ*. The same nerve after a normal saline bath of 1 hour, subsequently gave a marked CO_2 effect by 5 minutes tetanisation.
46	747	2 ,,	Primary augmentation . .	Greater augmentation of S.
		2 ,,	Primary diminution followed by secondary augmentation	Greater diminution of N.
47	752	1 ,,	Abolition followed by augmentation	Frog killed 6 hours, nerve in saline. Unequal and asynchronous effects on S. and N.
48	786	1 ,,	Primary augmentation	
50	869 (fig. 16)	2 ,,	Augmentation	Large fresh nerve; very slow stream of CO_2.

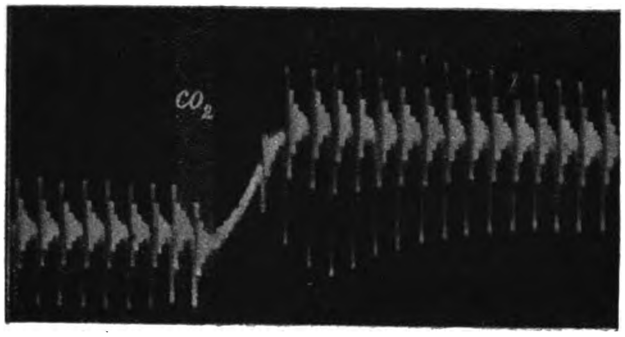
The conclusions to be drawn from these data (which were supplemented by many others unrecorded) are as follows :—

(1). *The typical effect of carbon dioxide upon normal nerve is a brief abolition followed by a prolonged augmentation of excitability* (figs. 14 and 17).

This result may nearly always be demonstrated, using fresh nerves of a recently killed healthy frog, and running CO_2 in full stream through the gas-chamber during 1 or 2 minutes.

With stale nerve, left in the animal killed 2 or 3 hours, or longer, 12 to 18 hours, the primary effect of CO_2 (diminution) is more marked and prolonged, the secondary effect (augmentation) is less marked (fig. 22). The negative deflection is large and rapidly declines.

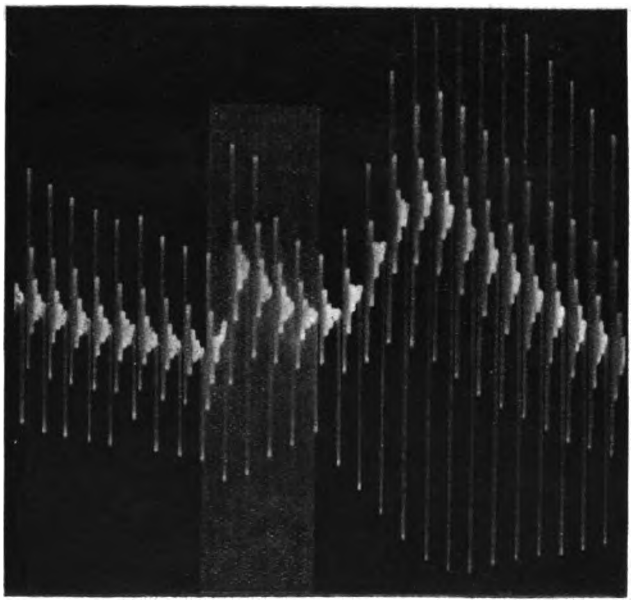
Fig. 14. (Obs. 200.)



Effect of CO_2 in full stream on normal freshly excised nerve. "Typical effect," viz., primary abolition followed by secondary augmentation of excitability.

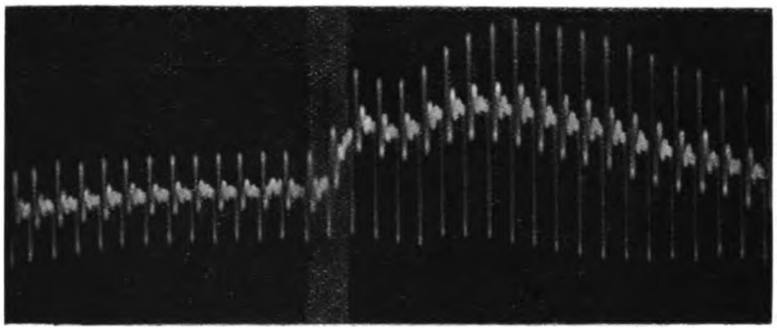
The gas-chamber containing the nerve measures 30 cub. centims. The nerve is tetanised each minute for 7½ seconds by ordinary make and break shocks at a frequency of about 70 per second, and a strength of 10 units of a Berne coil, supplied by two Leclanché cells. Interrupter in primary circuit. Time of passage of CO_2 through the nerve chamber indicated by the vertical bar across the record. Deflection before CO_2 = that of 0·0006 volt; after $CO_2 = 0$; 6 minutes later = 0·0012 volt. The "lag" of the CO_2 effect is probably due to diffusion time of the gas in contact with the nerve.

Fig. 15. (Obs. 537.)



Effect of a "moderate" quantity of CO_2 on nerve under similar conditions. Primary augmentation, diminishing; secondary further augmentation.

Fig. 16. (Obs. 869.)



Effect of a "small" quantity of CO_2 on nerve under similar conditions. Primary augmentation, in this instance, checked by a very slight diminution. Compare with figs. 5 and 6.

Fig. 17. (Obs. 633.)

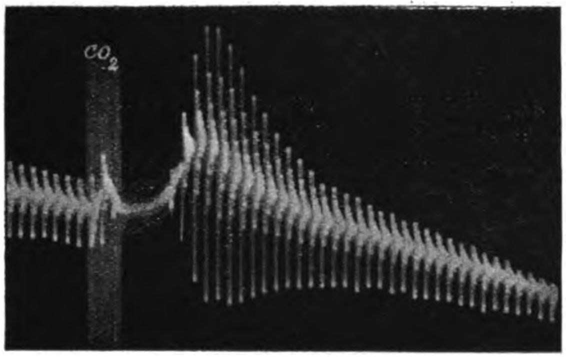


Fig. 18. (Obs. 652.)

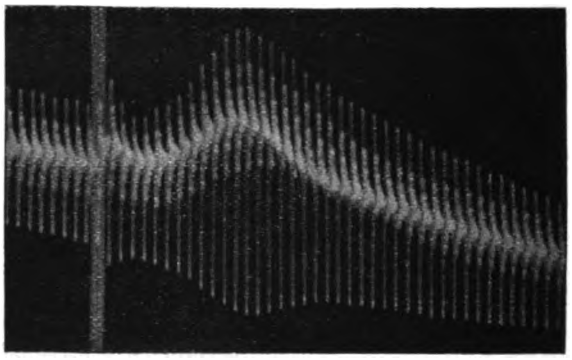
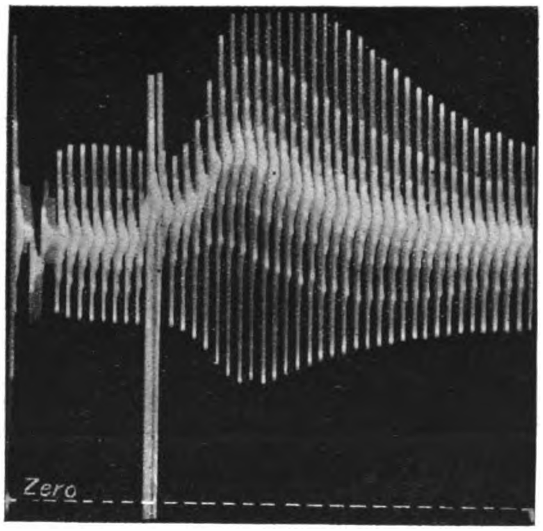


Fig. 19. (Ob. 674.)



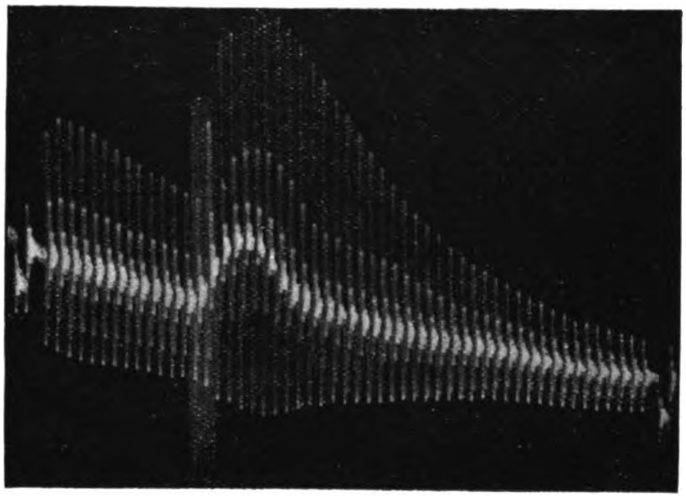
Figs. 17, 18, and 19. "Full," "medium," and "slight" effects of CO_2.

With stale nerve, kept in decinormal saline solution (0·58 per cent.) for 2 or 3 or more hours, the primary effect is less marked, and may only amount to a diminution short of complete abolition, the secondary effect is well marked.

(2). *The effect of a small amount of carbon dioxide upon normal nerve is a primary augmentation of excitability* (figs. 16, 19, 20).

Expired air, *e.g.*, containing 3 per cent. CO_2, produces primary augmentation (fig. 20).

Fig. 20. (Obs. 589.)



Effect of expired air.

(3). *The effect of a moderate amount of carbon dioxide is primary augmentation giving way to diminution and followed by secondary augmentation of excitability* (figs. 15 and 18).

The evident conflict taking place between movements in two opposite directions is in part due to an unequal action of CO_2 upon opposite processes in excited nerve. As will be shown later, CO_2 may, *at the same time*, give rise to augmentation of the negative deflection with diminution of the positive deflection.

The use of the indefinite terms "large," "moderate," and "small," is consequent upon the unavoidable variability in the physiological quality of excited nerve. A quantity of CO_2 that is large in relation to one nerve, giving the typical effect, may be moderate in relation to another nerve, or even small in relation to a third, giving primary augmentation. Such differences are partly connected with state of health, partly with the previous influences to which the nerves have been submitted, and partly with the mere bulk of nerve, in this last case by virtue of more gradual diffusion of the gas into thick than into thin nerves; the large nerves of German frogs, *e.g.*, required larger doses than the small nerves of English frogs to produce similar effects; on the other hand, the former gave remarkably distinct CO_2 effects in consequence of tetanisation. Strength of stimulation also influences the result; this strength, although as previously stated, taken with uniform coil distance, must vary with thickness of nerve and distance between exciting poles, and if the nerve is very thick or the distance between the poles less than usual, 10 units may possibly prove too high a stimulation strength to allow of the demonstration of complete abolition of excitability.

Fig. 21. (Obs. 671.)

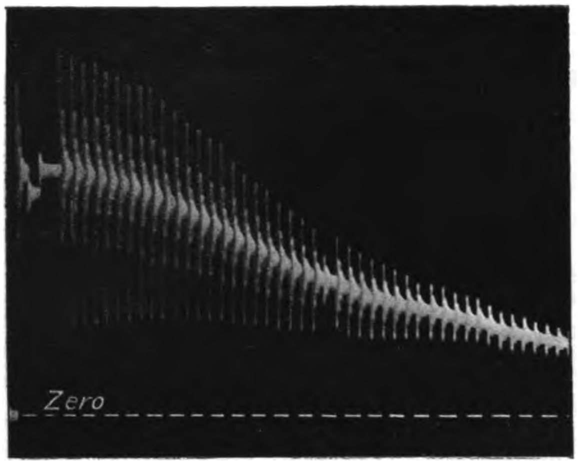
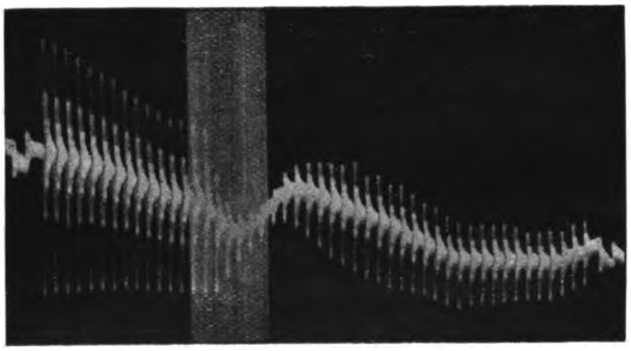


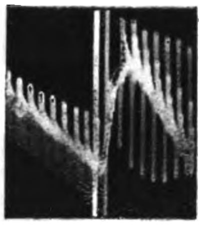
Fig. 22. (Obs 672.)



Records characteristic of nerve "carbonised" by prolonged sojourn in the living tissues of a pithed animal. The deflection is at first much larger than usual and declines more rapidly (fig. 21), the abolition caused by CO_2 is more prolonged than usual, and the after-augmentation is comparatively insignificant (fig. 22).

It is the excitability of the whole strand of protoplasm that is tested under the conditions of observation, the direct and the indirect or propagated molecular disturbance caused by stimulation, and modified by CO_2 or other gas. To determine whether the modification was more pronounced at the origin of the disturbance or at the part connected with the galvanometer, observations were taken with a gas-chamber carefully divided into two compartments, the nerve being passed through a small hole in the dividing wall, and the division made good by moist saline clay round the nerve and blocking the hole. CO_2 was then passed through one or other compartment; in both cases the characteristic modifications of excitability were produced, more pronounced however when the gas was passed through the compartment containing the leading-off electrodes than when it was passed through that containing the exciting electrodes. Similar results occurred with ether vapour.

Fig. 23. (Obs. 788.)



Currents of action, and effect upon them of CO_2, with the exciting and galvanometer circuit conjoined (as described on pp. 12, 13).

§ 2. *Action of Carbon Dioxide on Modified Nerve.*

The description hitherto given is that of the action of CO_2 upon normal nerve, giving the usual current of injury and excitatory negative deflection.

We have now to describe the action of carbon dioxide upon abnormal nerve, giving little or no current of injury, and an excitatory deflection in a positive direction.

This description is a necessary preface to any consideration of the evidence to be offered of a production of CO_2 within the nerve itself, but must itself be prepared by a summary description of the various kinds of excitatory deflections manifested by more or less profoundly modified nerve under regular excitations of regular strength (10 units) and duration (7½ secs.).

Deferring to a later stage (p. 45) any theoretical consideration as to the possible nature of a positive deflection, and simply to render possible an orderly description of the action of carbon dioxide, the following classification of nerve effects is adopted.

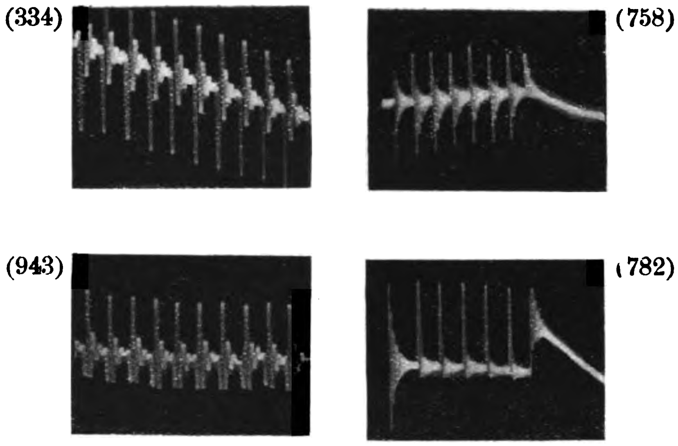
(1). During a first stage (fresh nerve) the galvanometric response to excitation consists in a large negative deflection succeeded by little or no positive after deflection.

(2). During a second stage (transitional nerve) the galvanometric response consists in a small negative deflection succeeded by a large positive after-deflection.

(3). During a third stage (stale nerve) the response consists in a positive deflection followed by a positive (rarely by a negative) after-deflection.

This division is, of course, more or less arbitrary, the transition from stage to stage is not sudden but gradual, as will be indicated more fully in Chapter IV., when we shall also inquire into the possible nature of positive deflections. For our present purpose the classification is indispensable.

Fig. 24.



Observations with the partially damped galvanometer, in 334 and 943, with an oscillation period of 12½ secs., and a swing-back = ⅔ the original swing; in 758 and 782, with an oscillation period of 8½ secs., and a swing-back = ⅓ the original swing.

No.	Effect.	Uncorrected after-effect.	Correction.	Corrected after-effect.
334	−10	+6·6	+6·6	0
943	− 4·5	+7	+3	+4
758	+ 6	−6	−2	−4
782	+12	−1	−4	+3

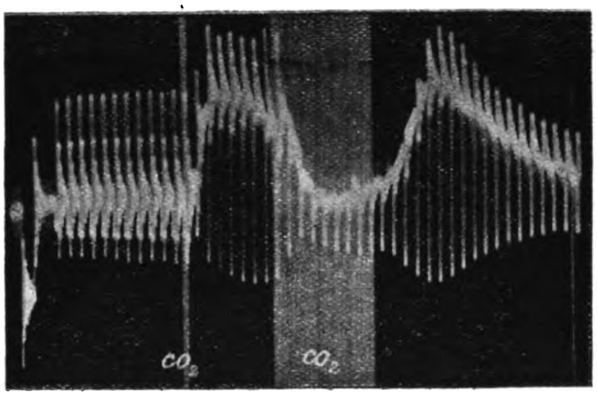
The action of CO_2 upon nerve in the first stage has been fully described above (p. 19).

The action of CO_2 upon nerve in the second stage is to augment the negative deflection and to diminish the positive after-deflection.

The action of CO_2 upon nerve in the third stage is to diminish the positive deflection or to substitute for it a negative deflection.

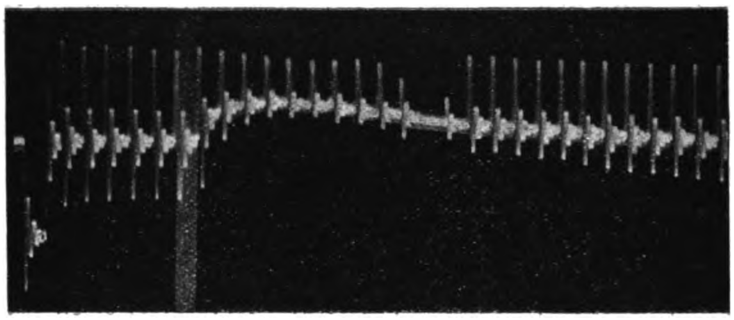
The data upon which these last two conclusions are based are contained in the following summary of observations.

Fig. 25. (Obs. 734.)



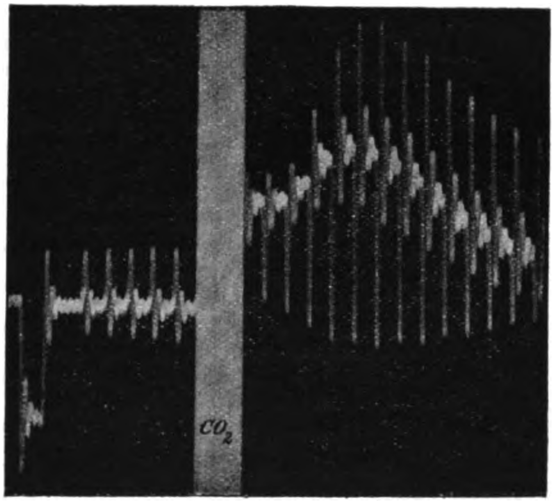
Influence of "little" and "much" CO_2 upon nerve in the second stage. (See Table B.)

Fig. 26. (Obs. 982.)



Influence of CO_2 upon nerve in the third stage; diminution of the positive effect.

Fig. 27. (Obs. 881.)



Influence of CO_2 upon nerve in the third stage; reversal of effect from positive to negative.

TABLE B.—Summary of Observations on the Action of Carbon Dioxide upon Modified Nerve.

Number.	Plate number.	CO_2.	
1	710 (fig. 35)	1 min. (150 cub. centims.)	The original deflection is a small S. effect, followed by a large N. after-effect. The first effect of CO_2 was to augment the S. and to diminish the N. Subsequently the S. and the N. were both increased.
2	711	10 mins. (1600 cub. centims.)	Same nerve. Similar results. The nerve had been kept for 18 hours in normal saline, and previously submitted to the action of ether vapour with a similar result, viz., simultaneous augmentation of S. and diminution of N. as the secondary result of etherisation.
3	727	2 mins. (600 cub. centims.)	Primary abolition followed by secondary augmentation, the augmentation of S. being greater than that of N. The nerve had been previously treated with HCl $n/40$ for 1 min.
4	734 (fig. 25)	100 cub. centims.	German frog. Nerve in normal saline for 3 hours. The original deflection is a small S. effect, followed by a large N. after-effect, giving place to a large S. followed by a small N., in consequence of the first dose of CO_2.
		1500 cub. centims.	The second and larger dose gives diminution of S. and abolition of N.
5	738	7 mins.	German frog. Nerve in normal saline for 15 minutes. Augmentation of S. with diminution of N.
6	742	7 mins. (twice)	Frog killed 3 hours; nerve left *in situ*. Primary effect { Slight diminution of S. effect. Greater diminution of N. after-effect. Secondary effect { Rapid, but slight augmentation of S. More gradual recovery of N.
7	743	4 mins.	German frog. Nerve for 4 hours in saline. Augmentation of S. with diminution of N., followed by augmentation of S. and slower augmentation of N.
8	744	4 mins.	English frog. Nerve 15 minutes in saline. Similar result to that of 743.
9	745	..	Second nerve of same frog. 1½ hours in saline. Similar result. N.B.—Ether subsequently gave a similar result.
10	747	..	English frog. Nerve 10 minutes in saline.
		1 min.	Augmentation of N. and of S.
		3 mins.	7 minutes later, diminution of S. and abolition of N.
11	752		Nerve in saline for 6 hours, and previously used for tetanus effect (751). The original deflection was s.N. The deflection after tetanus was S.N. The effect of CO_2 was primary abolition, followed by augmented S. before the reappearance of N.
12	786	1 min.	Primary augmentation of S. and N. S. is augmenting before N. N. is still augmenting when the augmentation of S. has begun to decline.
13	788 (fig. 23)	1 min.	Secondary coil and galvanometer in the same circuit. North deflection altered by CO_2 to a south deflection. Subsequently S. is diminishing while N. is increasing.
14	{837 838}	1 min.	North deflection abolished, gradually returning. Nerve 4 hours after excision, previously used for urea.

TABLE B.—Summary of Observations on the Action of Carbon Dioxide upon Modified Nerve—(continued).

Number.	Plate number.	CO_2.	
15	839	2 mins.	North deflection gives way to small north followed by south after-deflection.
16	841 842	2 mins.	Nerve 8½ hours in saline. North replaced by south deflection, and subsequently returning.
17	843 (fig. 41)	4 mins.	Same nerve. Similar result.
18	844	4 mins.	Same nerve. Similar result.
19	851	1 min.	Nerve 1½ hours after excision, previously used for urea. Augmentation of the quotient S/N.
20	859 (fig. 31)	3 mins.	Nerve left for 6 hours in blood-serum, then used for another 6 hours for various experiments (CO_2, acetone vapour, tetanus). N.n. temporarily replaced by S.n. (The same nerve previously tested by 5 minutes' tetanisation gave a similar result; Obs. 858, fig. 30).
22	871	1 min.	1 hour after excision. Typical increase by "little" CO_2 in expired air. The same nerve 8 hours later gave a north deflection that was diminished by 5 minutes' tetanus (see Obs. 874, fig. 45).
23	877	1 min.	Conversion of s/N into S/n.
24	881 (fig. 27)	2 mins.	Nerve left for 15 hours in saline. Replacement of N. by S.
25	882	2 mins.	Same nerve. Diminution of N.
26	886	2 mins.	Nerve left for several hours in saline. Conversion of s/N into S/n.
27	935	4 mins.	Nerve left for 10 hours in saline. Variation s/N. Augmentation of s. with diminution of N., followed by diminution of s., and subsequently by augmentation, *i.e.*, typical effect of CO_2 in "moderate" amount.
28	982 (fig. 26)	1 min.	Nerve 2 hours after excision, previously used for creatine; diminution of N. deflection.
29	983	4 mins.	Same nerve. Abolition of N. deflection. Reappearance of S., subsequently S.N., s.N., n.N. (The same nerve shortly afterwards gave the original deflection N., which was diminished by 5 minutes' tetanisation (Obs. 984, fig. 32). An hour later the north variation was reversed by tetanisation for 13 minutes (Obs. 986).
30	990	1 min.	Nerve 2 hours after excision; previously tested by CO_2, and by sarcosin. Diminution of N. deflection. (The same nerve previously tested by 5 minutes' tetanisation, exhibited diminution of the N. deflection (Obs. 989).
31	992	1 min.	Nerve kept for 3½ hours in saline, and previously used for tetanus (991) giving a *s.* deflection, followed by a N. after-deflection. Subsequently to CO_2 the s. deflection is greatly augmented, the N. after-deflection is relatively diminished.
32	993	1 min.	Same nerve about half hour later gives o.N. deflection and after-deflection, converted to S.N. by CO_2. (See Obs. 991 and 994 in Table C.)
33	2006	1 min.	Nerve 6 hours in saline. Variation s.N. before CO_2, which produced diminution of s., followed by augmentation, and still greater diminution of N. (The same nerve, previously tested by 5 minutes' tetanisation, exhibited a similar temporary diminution of s.; Obs. 2005).

TABLE B.—Summary of Observations on the Action of Carbon Dioxide upon Modified Nerve—(continued).

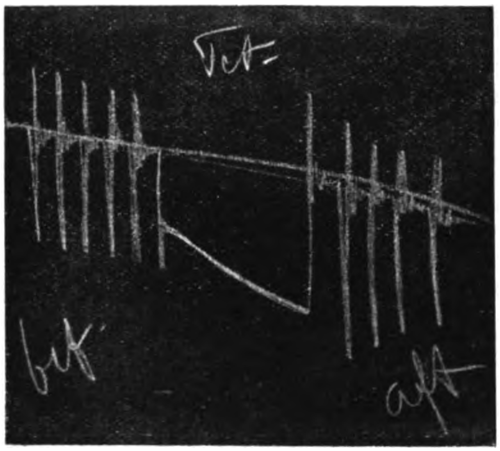
Number.	Plate number.	CO_2.	
34	2067	1 min.	Nerve 30 hours in saline (Jan. 11, 1896). N. temporarily replaced by S. deflection. (The same nerve, previously tested by 5 minutes' tetanisation, gave only a diminution of N.; Obs. 2066; in other respects the two records are precisely similar.)
35	2073	2 mins.	Nerve kept for 2 hours in 5 per cent. lactose solution, and giving a N. deflection, which is reversed to S. by CO_2. (The same nerve gave a similar reversal in consequence of 5 minutes' tetanisation; Obs. 2072.)
36	2075	2 mins.	Same nerve; similar result, viz., reversal (Obs. 2074 gave similar result by 5 minutes' tetanisation of the same nerve).
37	2080	2 mins.	Nerve kept for 4 hours in lactose solution, 5 per cent., and giving a deflection s.N. Augmentation of *s.* in consequence of CO_2. (The same nerve gave a similar but less marked effect, viz., augmented s., in consequence of 5 minutes' tetanisation.)
38	2082	2 mins.	Nerve kept for 8 hours in saline, giving a N. deflection, which is temporarily reversed to S. after CO_2. (The same nerve gave an augmentation of the N. deflection after 5 minutes' tetanisation; Obs. 2081.)
39	2241	..	Dead-beat galvanometer. Nerve kept for ¾ hour in saline. Great augmentation of S. deflection; subsequent appearance of N. after-deflection.
40	2242	..	Same nerve continued. The response is now s.N., and is temporarily changed to S.o. by CO_2.
41	2248	..	Dead-beat galvanometer. Nerve in saline for ¼ hour. Great augmentation of S. deflection by CO_2.
42	2249 (fig. 67)	..	Dead-beat galvanometer. Nerve in saline for 1¾ hours. Great augmentation of S. deflection, subsequent appearance of N. after-deflection.
43	2251	1 min.	Dead-beat galvanometer. Fresh nerve. Original effect S.n.; augmentation of S. and abolition of n. by CO_2, subsequently augmentation of n.
44	2253	..	March 12, 1896 (Lecture experiment). Original variation s., augmented by little CO_2; augmentation subsequently abolished by more CO_2 and followed a few minutes later by secondary augmentation.
45	2256	3 mins.	Dead-beat galvanometer. Experiment made twice at interval of 10 minutes. In each case primary diminution of S. deflection followed by secondary augmentation.
46	2257	..	Dead-beat galvanometer. Nerve left *in situ* for 12 hours before excision. Primary diminution of S., not followed by secondary augmentation.
47	2268	2 mins.	Dead-beat galvanometer. Nerve in saline for 1 hour. Original effect s.n.; primary abolition, secondary augmentation.
48	2274	1 min.	Dead-beat galvanometer. In saline 4 hours; fresh transverse section. Primary augmentation of S deflection only, soon followed by augmentation of n. after-deflection.
49	2276	1 min.	Same nerve; 2 hours later the deflection is n., temporarily abolished and reversed to s. by CO_2.
50	2277	1 min.	The same nerve, 15 hours later, gives a deflection s. (without new transverse section, diminished by CO_2).

CHAPTER III.—PRODUCTION OF CO_2 IN TETANISED NERVE.*

§ 1. *Evidence in Normal Nerve.*

Evidence of chemical and thermic change in active nerve, analogous with that obtained in the case of active muscle, does not as yet exist That now offered of a production of CO_2 within isolated nerve rests upon our knowledge of the effects produced upon nerve by CO_2 reaching it from without. It will be shown in the present communication that tetanised nerve manifests alterations identical in kind with the alterations characteristic of the action of CO_2. It is, perhaps, permissible to state that the alterations were forecast by the following argument and diagram (fig. 28) before they were verified by experiment (fig. 29).

Fig. 28.



Hypothesis.

CO_2 in very small quantity produces an augmentation of the negative, or south deflection, and the delicacy of the reaction is extreme. If, then, tetanisation of nerve is attended with any CO_2 production, we may expect that such CO_2, arising within the nerve itself, will effect the characteristic augmentation. The negative deflection should be greater after a prolonged tetanus, the augmentation should gradually diminish with the presumable dissipation of CO_2; moreover, the negative deflection of the tetanus itself should increase with the presumable evolution of CO_2 during its progress—as in the diagram (fig. 28).

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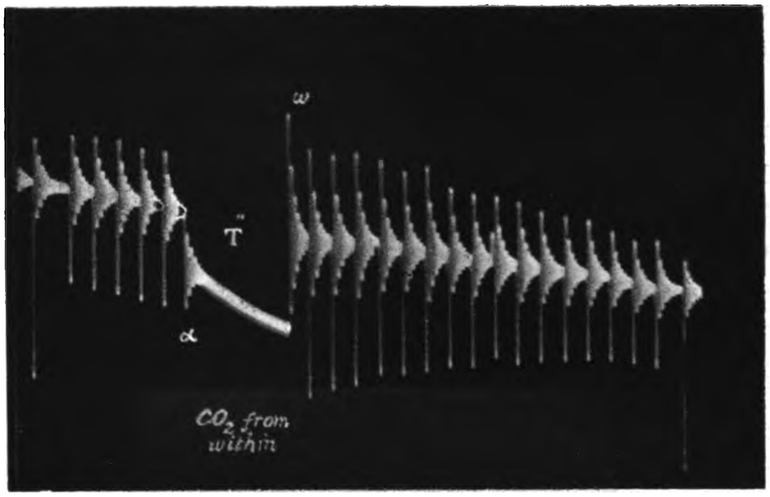
* In view of the criticism to which the above title has given rise, to the effect that no carbon dioxide has been separated and identified, it appears desirable, if somewhat superfluous, to premise that no CO_2 gas has been collected and identified by chemical tests, and that the evidence offered rests entirely upon the physiological test afforded by the nerve itself in various states; the nerve serves as the reagent, reacting in all particulars to tetanisation as it does to CO_2, from which, as in the case of any other test (with more or less certainty, according to the circumstances under which the test is made), the inference is drawn that CO_2 is produced during tetanisation, on the principle that, under similar circumstances, similar effects are due to a similar cause.

The forecast was borne out in all its features, as may be seen in fig. 29.

Fig. 29. (Obs. 675.)



Verification.

§ 2. *Evidence in Modified Nerve.*

Confirmatory evidence towards the same conclusion is afforded by the following complementary experiments upon nerve in the second and third stages.

As has been shown above (p. 25), the typical effect of CO_2 upon a reversed excitatory effect (north or positive) of the third stage is to restore that reversed effect to its original character as a (south) negative deflection.

Tetanisation effects a similar reversal of the positive effect.

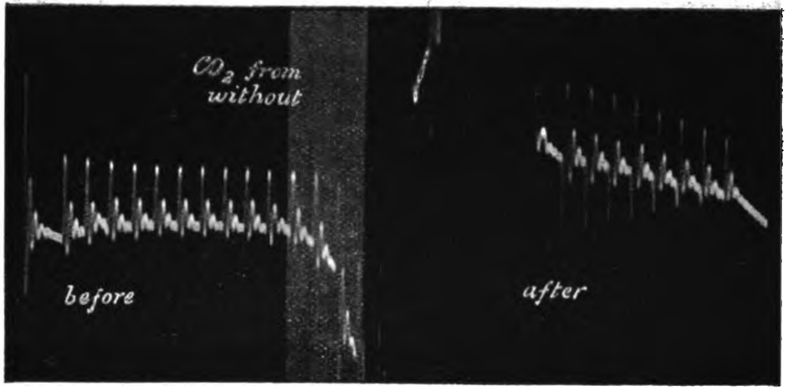
Fig. 30 exhibits this reversal of a positive (north) deflection, and its replacement by a negative (south) deflection, in consequence of CO_2, passed through the gas-chamber.

Fig. 31 exhibits upon the same nerve, under similar conditions, the similar effect of tetanisation, presumably by reason of CO_2 evolved within the nerve itself.

In addition to these two representative experiments, two further experiments, which, however, are no more than varieties of the second, afford corroborative evidence.

As has been stated above (p. 25), the effect of carbon dioxide upon the north or positive deflection of the third stage does not always amount to the complete reversal of deflection, but only to its diminution; a similar effect may then be produced by tetanisation. The apparently contradictory nature of this result as compared with that obtained on nerve of the first stage, viz., diminution of an effect of excitation, is in reality confirmatory evidence; in this, as in the other cases, a negative sum or process has been augmented (or a positive sum or process has been diminished) as an effect of CO_2 applied from without or arising from within.

Fig. 30. (Obs. 859.)



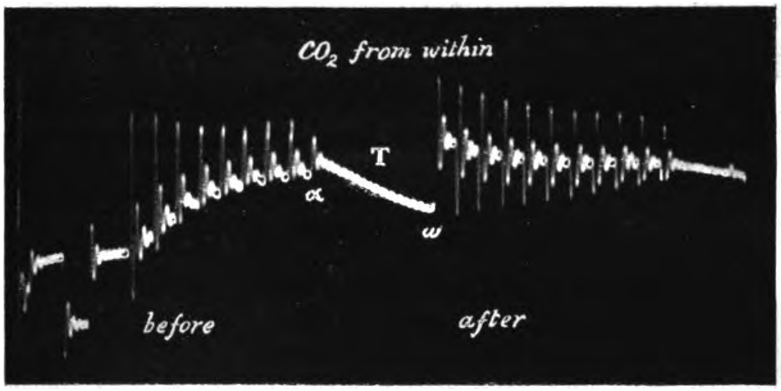
Nerve in third stage after half an hour's rest. Influence upon the deflection of a slow stream of CO_2.

Before CO_2.—The deflections are north north, consisting of a positive effect followed by a positive after-effect.

During the passage of CO_2 the spot fell off plate south. Subsequently, having been readjusted north, it rose off plate north.

After CO_2.—Large negative effect diminishing, smaller positive after-effect increasing. Half an hour later the deflections were again north north.

Fig. 31. (Obs. 858.)



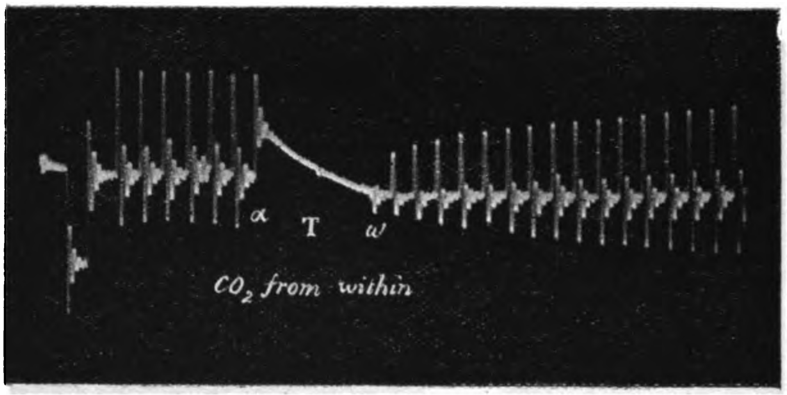
Same nerve giving a positive effect, followed by a positive after-effect. North north.

Before Tetanus.—Positive effects rapidly diminishing. Positive after-effects summating and causing the base line to rise. The last three effects exhibit a slight negative effect at the end of each excitation, interposed between the positive effect and the positive after-effect.

During Tetanus.—Positive deflection becoming increasingly negative. The first deflection at the commencement of the tetanus is north, the first deflection at the end of the tetanus is north.

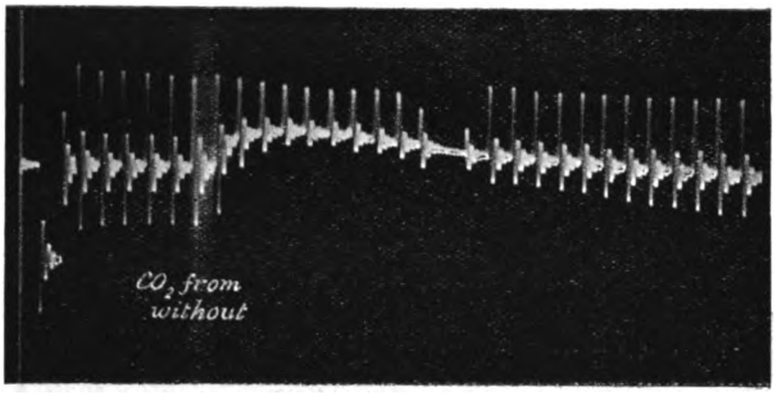
After Tetanus.—Large negative effects diminishing, smaller positive after-effects increasing. After a subsequent half hour of repose, the negative effects had vanished, the deflection had again become north north.

Fig. 32. (Obs. 984.)



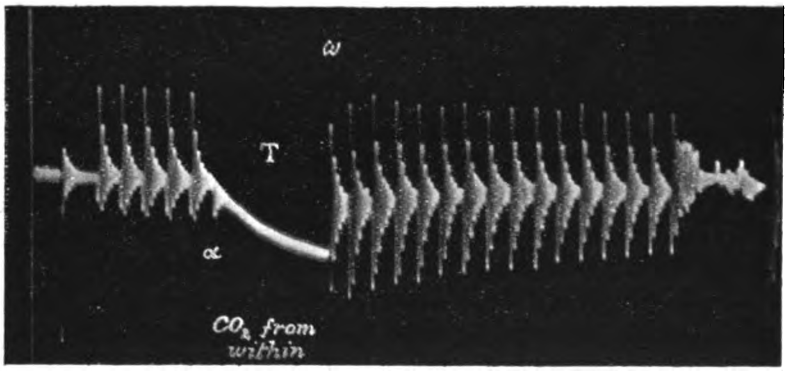
Influence of tetanisation upon nerve in the third stage; diminution of the positive effect.

Fig. 33. (Obs. 982.)



Influence of carbon dioxide upon nerve in the third stage; diminution of the positive effect. (The irregularity of response from the 16th to 18th minute is due to irregularity of the stimulating apparatus.)

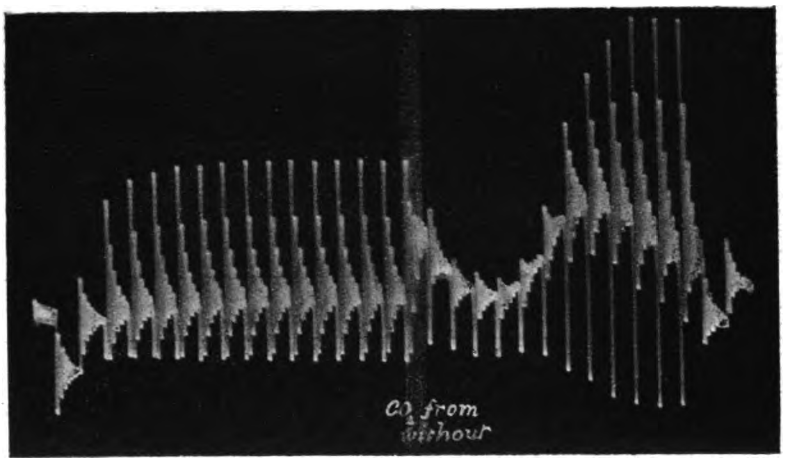
Fig. 34. (Obs. 762.)



Influence of tetanisation upon nerve in the second stage, giving the response *s*.N., viz., small negative effect followed by large positive effect; augmentation of the negative effect.

When further, as in the case in the second stage, the effect of CO_2 upon a small negative or south deflection followed by a large positive or north after-deflection, is to reverse the relative magnitudes of the two deflections, a similar effect is produced by tetanisation.

Fig. 35. (Obs. 710.)



Influence of carbon dioxide upon nerve in the second stage, giving the response *s*.N.; augmentation of the negative effect.

There is, in short, complete similarity between the effects of external CO_2 in various states of nerve and those of the presumably internal CO_2 of tetanisation during these same various states; a correspondence so close, that the evidence may be held as conclusive. Whether disintegration products other than CO_2 are produced by nerve-tetanisation is of course neither affirmed nor denied.*

The accompanying summary (Table C) contains the experimental data upon which the general conclusion is based that CO_2 is produced in tetanised nerve.

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* As will be shown in Chapter IV., the principal effect of CO_2 upon anelectrotonic and katelectrotonic currents is augmentation, a similar effect is produced by prolonged tetanisation. But here, as in the case of the negative variation, quantity of CO_2 in relation to state of nerve has to be taken into account, and my experiments in this direction are not sufficient to justify categorical statements.

TABLE C.—Summary of Data in Evidence of the Production of Carbon Dioxide in Normal and in Modified Nerve.

Under the heading " Character of the Deflection " is also given, when possible, that of the after-deflection.

Under the heading α is given the deflection at the beginning of the prolonged tetanus, under the heading ω that at its end.

Numerical measurements of several of the observations in this table, as well as in Table B, are given in Table D.

The time of year at which observations were taken may be ascertained by ~~reference to the " time-table " at the~~ end of the paper.

No.	Plate No.	Conditions of experiment.	Duration of tetanisation.	Character of deflection before tetanisation.	α.	During tetanisation.	ω.	Character of deflection after tetanisation.	Remarks.
			minutes.						
1	675 (fig. 29)	Nerve in saline for 1 hour after excision	5	S.N.	S.	Increasing	N.	S.N.	Table D.
2	676	A few minutes after excision . .	10	S.N.	S.	"	N.	S.N.	
3	677	Nerve left in pithed frog for 1 hour before experiment	10	S.N.	S.	"	N.	S.N.	Declining normal.
4	678	Same nerve as in 676; nerve put aside for 1 hour in saline	10	S.N.	S.	"	? S.	S.N.	
5	679	A few minutes after excision . .	10	S.N.	S.	"	N.	S.N.	Declining normal, more especially as regards the N. after deflection.
6	680	Nerve in saline for 2 hours after excision	10	S.N.	S.	"	? S.	S.N.	
7	689	Nerve in saline for $\frac{3}{4}$ hour after excision	20	S.N.	S.	Increasing S.	? S.	S.N.	Augmented deflection S., diminished after deflection N., subsequent to tetanisation.
8	737	2 hours in saline; previously used for ether experiment (735)	5	S.N.	. .	"	. .	S.N.	
9	741	1 hour in saline; previously tested by CO_2 (740)	5	S.N.	S.	"	N.	S.N.	Typical effect of CO_2 in Obs. 740 on same nerve.
10	751	6 hours in saline	5	n.N.	. .	Decreasing N.	. .	S.N.	Reversal. Typical effect of CO_2 in Obs. 752 on same nerve.
11	758	$5\frac{1}{2}$ hours in saline	5	N.S.	N.	"	s.N.	s.N.	Reversal from N. to s.
12	761	4 hours in saline; previously tested by oxalic acid n/20	5	S.	S.	Increasing S.	N.	S.	Augmentation of S.
13	762 (fig. 34)	6 hours in saline	5	s.N.	s.	"	N.	S.N.	Augmented S.

TABLE C.—Summary of Data in Evidence of the Production of Carbon Dioxide in Normal and in Modified Nerve—(continued).

No.	Plate No.	Conditions of experiment.	Duration of tetanisation.	Character of deflection before tetanisation.	α.	During tetanisation.	ω.	Character of deflection after tetanisation.	Remarks.
			minutes.						
14	782	10 minutes in saline, then heated to 41°, then record taken	5	N.N.	N.	Decreasing N.	S.	N.	The original deflection before heating was S.n. (Obs. 781).
15	857	6½ hours in serum; previously tested by acetone vapour	5	N.N.	s.	"	N.	s.N.	Acetone vapour had had no apparent effect (Obs. 855).
16	858 (fig. 30)	Same nerve after ½ hour rest . .	5	n.N.	n.	"	N.	s.N.	
17	862	3 hours in saline; previously tested by urea 2 per cent. solution	5	s.N.	s.	Increasing S.	N.	S.N.	
18	863	Same nerve	5	s.N.	s.	"	N.	S.N.	
19	865	" "	5	s.N.	s.	"	N.	S.N.	
20	866	" "	5	s.N.	s.	"	N.	S.N.	
21*	873	3 or 4 hours in saline; previously used for ether experiment (870)	5	N.	N.	Decreasing N.	S.	N.	
22	874 (fig. 45)	Same nerve	5	N.	N.	"	S.	N.	
23	875	In saline a few minutes	5	S.	S.	Increasing S.	N.	S.	
24*	876	Same nerve	5	S.	S.	"	N.	S.	Repeated twice; increased S. after the first tetanus, decreased S. after the second. CO_2 subsequently gave marked increase.
25*	878	In saline 13 hours	7	N.	N.	Decreasing N.	S.	N.	
26	880	In saline 1 hour	5	o.N.	o.	Increasing S.	n.	S.N.	Reversal.
27	882	Same nerve 1 hour later. . . .	5	N.	N.	Decreasing N.	S.	N.	Very little alteration by tetanus, and only diminution of N. by CO_2.
28*	883	Same nerve	5	S.N.	S.	Increasing S.	n.	s.	
29*	885	" "	5	N.	N.	Decreasing N.	S.	N.	Repeated twice; with augmentation of N. in each case.
30	898 (fig. 46)	Nerve previously tested by sarcosin solution 1 per cent. (897)	5	N.	N.	"	N.	S.N.	Reversal.

TABLE C.—Summary of Data in Evidence of the Production of Carbon Dioxide in Normal and in Modified Nerve—(continued).

No.	Plate No.	Conditions of experiment.	Duration of tetanisation.	Character of deflection before tetanisation.	α.	During tetanisation.	α'.	Character of deflection after tetanisation.	Remarks.
			minutes.						
31*	905 (fig. 36)	Nerve previously tested by creatin solution 2 per cent. (902–3)	10	N.	N.	Decreasing N.	S.	N.	Augmented N. Obs. 906 with CO_2 on the same nerve is also exceptional.
32	912 (fig. 37)	In saline 15 hours.	10	s.N.	s.	Increasing S.	N.	s.n.	Diminished s., also diminished after-effect N.
33	928	Nerve previously tested by muscle extract (926, 927)	5	S.N.	S.	„	N.	S.N.	Great augmentation of S. See Table D.
34	929	Same nerve	5	s.n.	s.	„	N.	S.N.	Great augmentation of S. See Table D.
35	934	In saline 10 hours; previously tetanised for 1½ hour	5	S.N.	S.	„	N.	S.N.	No appreciable effect; on the same nerve CO_2 for several minutes gave only augmented S.
36	937	In saline 24 hours	5	S.N.	S.	„	N.	S.N.	Augmented S.
37	940	„ 14 „	5	S.N.	S.	„	N.	S.N.	Slight augmentation of S.
38	941	„ 1½ „	30	S.N.	S.	„	N.	S.N.	Augmented S.
39*	942	Same nerve	5	N.	N.	Decreasing N.	S.	N.	Augmented N.
40	946	In saline 3 hours; previously used for serum-albumin (945)	5	s.N.	s.	Increasing S.	N.	S.N.	Augmented S.
41	950	Previously used for diabetic sugar (949)	5	n.s.	n.	Decreasing N.	S.	n.s.	Diminished N.
42	954	2 hours after excision; previously used to test diabetic sugar (951–2–3)	5	n.s.	n.	„	S.	n.s.	Diminished N.
43	955	Same nerve	5	N.S.	N.	?	?	n.s.	Diminished n. deflection; less, if at all, diminished S. after-deflection.
44	958 (fig. 39)	In saline 5 hours; previously used to test diabetic sugar (956–7)	5	s.N.	S.	Increasing S.	N.	S.n.	
45	960 (fig. 42)	In saline 10 hours; previously used for diabetic sugar	5	o.N.	O.	„	N.	S.n.	
46	984 (fig. 32)	Previously tested by creatin 2 per cent. and by CO_2	5	N.	N.	Decreasing N.	s.	n.	Compare with Obs. 982, fig. 33.

TABLE C.—Summary of Data in Evidence of the Production of Carbon Dioxide in Normal and in Modified Nerve—(continued).

No.	Plate No.	Condition of experiments.	Duration of tetanisation.	Character of deflection before tetanisation.	α.	During tetanisation.	ω.	Character of deflection after tetanisation.	Remarks.
47	985	Same nerve	minutes. 5	N.	N.	Decreasing N.	s.	n.	Similar effect, viz., diminution of N.
48	986	Nerve 14 hours in saline . . .	12	N.	N.	”	N.	S.	Reversal.
49	989	Previously tested by sarcosin 5 per cent.	5	N.	N.	”	?	n.	Diminution of N. The same nerve gave similar diminution by CO_2. Obs. 990.
50	991	2½ hours in saline	5	s.N.	s.	Increasing S.	N.	S.N.	Augmentation of S. Similar result on the same nerve by CO_2; Obs. 992; about 1 hour later o.N. deflection altered to S.n. by CO_2; Obs. 993. This series, 991-2-3-4, illustrates very plainly the identical results of tetanus and of CO_2.
51	994	Same nerve	5	o.N.	o.	”	N.	s.N.	
52	2003	2 hours in saline; previously tested by propionic acid, n/20	5	S.	S.	”	n.	S.	
53	2004	6 hours in saline	5	s.N.	s.	?	N.	S.N.	
54*	2005	Same nerve	5	S.N.	S.	Increasing S.	N.	s.n. S.N.	Diminution of S. followed by augmentation. Similar effect by CO_2 in next observation on same nerve: Obs. 2006.
55*	2030	In saline 18 hours; previously tested by propionic acid, n/50 and n/40 (2026–7)	5	S.S.	S.	”	? N.	S.N.	CO_2 on the same nerve subsequently gave the usual effect; Obs. 2031.
56	2054	In saline 19 hours (Jan. 12, 1896)	5	S.	S.	”	N.	S.	Augmentation of S.
57	2055	Same nerve	5	S.	S.	”	N.	S.	Augmentation of S.
58	2057	Same nerve	5	S.	S.	”	N.	S.	Augmentation of S.
59	2060	Same nerve left in saline 12 hours longer	5	S.	S.	”	N.	S.	Augmentation of S.
60	2065	In saline 26 hours (Jan. 13, 1896)	5	N.	N.	Decreasing N.	N.	n.	Diminution of N.

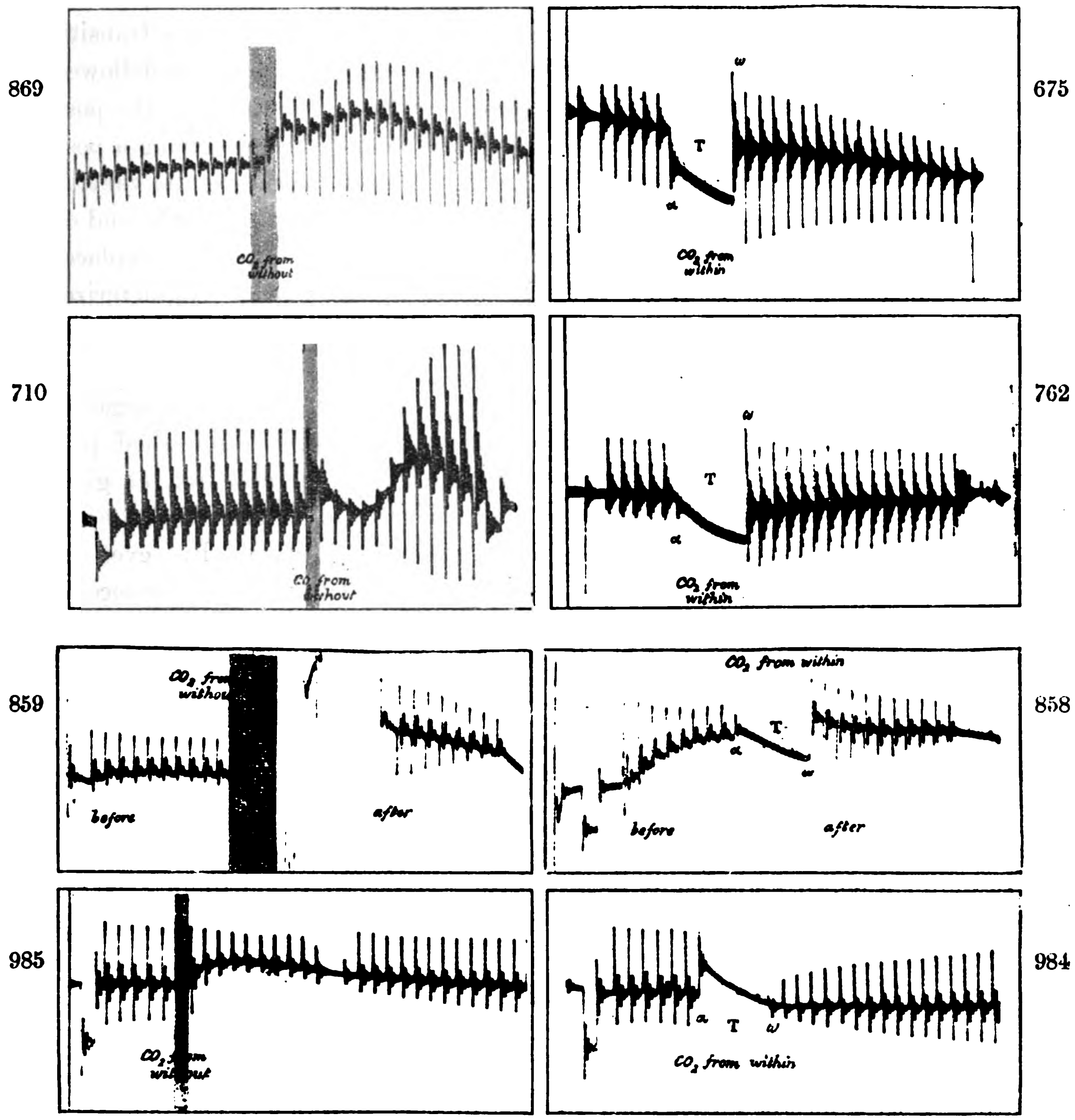
TABLE C.—Summary of Data in Evidence of the Production of Carbon Dioxide in Normal and in Modified Nerve—(continued).

No.	Plate No.	Conditions of experiment.	Duration of tetanisation.	Character of deflection before tetanisation.	α.	During tetanus.	ω.	Character of deflection after tetanisation.	Remarks.
			minutes.						
61	2066	Same nerve	5	N.	N.	Decreasing N.	N.	n.	The same nerve, subsequently tested by CO_2, gave reversal to s. soon followed by return to n. and N.; Obs. 2067.
62	2072	After lactose 5 per cent. for 1¼ hour	5	n.N.	n.	"	N.	s.N.	Reversal. Similar effect by CO_2 in Obs. 2073.
63	2074	9 hours in saline	5	n.N.	n.	"	N.	S.N.	Reversal. Similar effect by CO_2 in Obs. 2075.
64	2079	After 4 hours in lactose solution 5 per cent.	5	S.N.	S.	Increasing S.	N.	S.N.	Augmentation of S. Similar effect by CO_2 in Obs. 2080.
65*	2081	8 hours in saline	5	N.	N.	?	?	N.	Augmentation of N. CO_2 gave reversal from N. to S.; Obs. 2082.
66*	2084	Same nerve as in 2079, left in saline 18 hours longer; new transverse section	5	S.N.	S.	Decreasing S.	N.	s. Increasing.	Diminution of S. (The strength of tetanisation was 100 units.)
67	2258	10 minutes in saline	5	S.n.	s.	Increasing S.	N.	S.n.	S. deflection increased; n. after-deflection diminished. Dead-beat galvanometer.
68	2262	24 hours in saline; new transverse section	5	S.n.	S.	Steady deflection	N.	S.n.	S. deflection increased; n. after-deflection diminished. Dead-beat galvanometer.
69	2271	1 hour in saline	5	S.n.	S.	Increasing S.	N.	S.n.	Augmented S.; hardly any alteration of the after-deflection n. Dead-beat galvanometer.

NOTE.—In several of the above observations the same nerve has been tested by tetanisation and by CO_2 without removal from the electrodes or other disturbance; this has been the case, *e.g.*, in 740–741, 751–752, 858–859 (figs. 30–31), 982–984 (figs. 32–33), 989–990, 2005–2006, 2072–2073, 2074–2075, 2079–2080, 2081–2082.

On review of the foregoing data, it will be seen that the great majority of experiments gave clear and unambiguous results, but that in some (indicated by an asterisk in Table C) the results have been apparently ambiguous. These require commentary.

Fig. 35A.



Summary of observations presenting typical effects of CO_2 and of tetanisation upon nerve in the three states alluded to in text.

Action of CO_2 (869) and of tetanisation (675) upon nerve of the 1st stage.
„ „ (710) „ „ (762) „ „ 2nd stage.
„ „ (859) „ „ (858) „ „ 3rd stage, "clear effect."
„ „ (985) „ „ (984) „ „ „ "disguised effect."

§ 3. *Ambiguous Phenomena in Modified Nerve.*

The typical and regular result with a fresh nerve (giving a large negative deflection during excitation) is as represented by Obs. 741 (fig. 29), an augmentation of the negative deflection. And as regards the tetanus itself, the deflection at its commencement is negative, at its end positive.

Similar results are obtained with a nerve in what has been termed a transitional state, neither "fresh" nor "stale" (giving little or no negative deflection followed by a large positive after-deflection); the negative deflection is increased and the positive after-deflection less increased, or diminished. With "stale" nerve (giving a positive deflection followed by a positive or a negative after-deflection) the results vary.

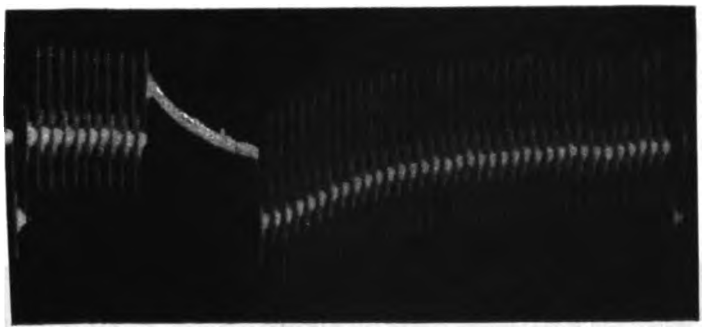
a. The deflection at the beginning of tetanus is positive and that at the end of the tetanus is positive, in which case a positive deflection before tetanus is replaced by a negative deflection after tetanus. This is the case that may be characterized as giving a "clear" effect, viz., reversal from N. to S., in consequence of CO_2 and of tetanisation.

b. The deflection at the beginning of tetanus is positive, at its end negative, in which case a positive deflection before tetanus remains as a diminished positive deflection after tetanus. This is the case that has been characterised as giving a "disguised" effect of CO_2 and of tetanisation, inasmuch as it presents an apparent exception to the rule that CO_2 augments the excitatory deflection. But even in this in some other respects anomalous case of "stale" nerves, the result may be recognized as offering no exception to the rule that CO_2 augments the negative deflection (or diminishes the positive deflection).

A noteworthy point in connection with the long tetanic deflection is that it always (at the stimulation strength of 10 units) progressively augments. It has only been with excessive strength of stimulation (100 units) that an augmentation has given way to diminution.

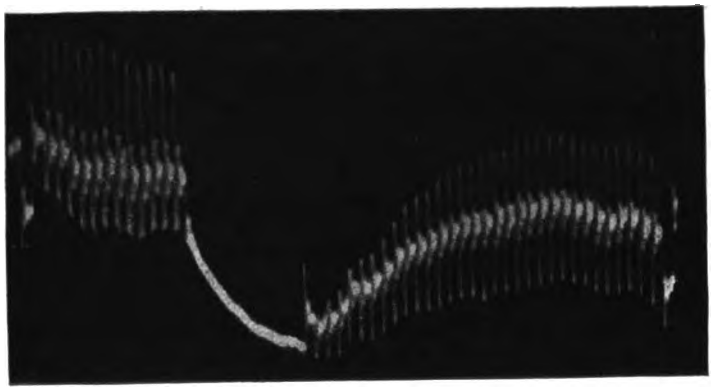
Occasional exceptions are met with to the rule that after the prolonged tetanus (at 10 units) a south variation is increased, or a north variation diminished; these have been distinguished in the table of data by an asterisk, and are illustrated in figs. 36 and 37. The possible significance of these exceptions where there is diminution of a south deflection, is indicated by the fact that a similar diminution can sometimes be demonstrated by using stimulation of excessive strength (fig. 38). Whether this diminution is to be regarded as a more profound effect of CO_2 in larger quantity, or as a fatigue effect, must be left an open question. The fact that the exceptional result may appear in the form of an augmented north deflection seems to be opposed to the latter alternative, and the key to these, in any case infrequent, peculiarities will probably be found in the peculiar differences of action of CO_2 in various quantities upon the deflection and after-deflection of nerve in various states; 905 exhibits this exceptional effect on a north variation, 912 on a south variation, and 2068 exhibits the dependence of the latter upon strength of tetanisation.

Fig. 36. (Obs. 905.)



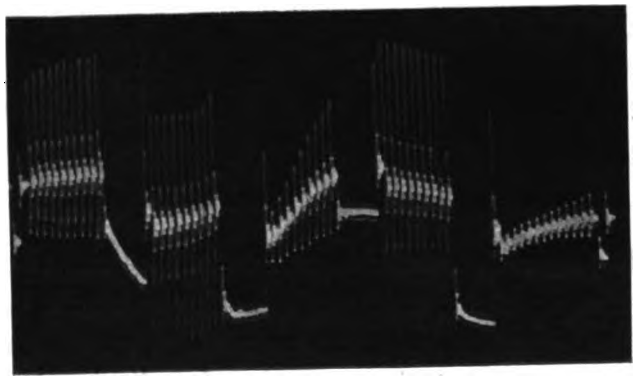
Nerve of the third stage. Exceptional effect of prolonged tetanisation. Augmentation of the positive deflection.

Fig. 37. (Obs. 912.)



Nerve of the second stage. Exceptional effect of prolonged tetanisation. Diminution of the negative deflection.

Fig. 38. (Obs. 2068.)



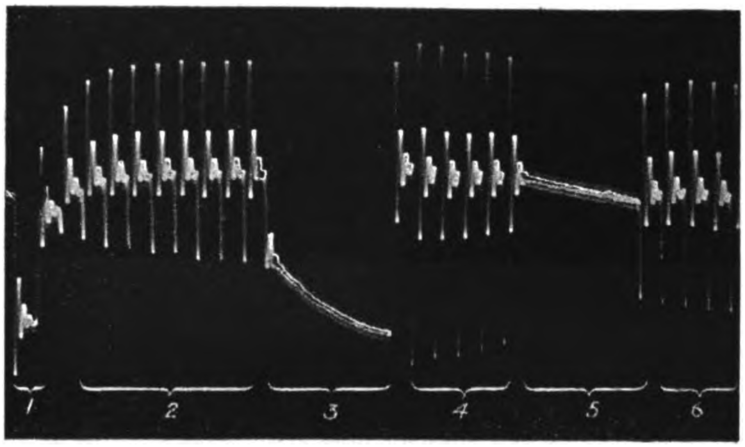
T 10↑ T 100↑ T 10↓ T 100↓

Nerve of the second stage. Augmented negative effect in consequence of weak tetanisation (10 units, both directions of coil). Diminished negative effect in consequence of strong tetanisation (100 units, both directions of coil).

§ 4. *The Staircase Effect.*

Under the conditions of these observations, isolated nerve nearly always exhibits the "staircase phenomenon" familar to physiologists in the contractile tissue of Medusa, in the Frog's heart, and in skeletal muscle. If the record of a normal series of deflections is commenced without preliminary testing, each deflection slightly (in some cases markedly) exceeds its predecessor; the increment progressively diminishing so that a line passing through the culminating points is concave to the line of rest, and the S. : N. quotient gradually increases. In the case of nerve the phenomenon is in lesser degree a tetanus effect, similar to that described and considered above, viz., presumably a CO_2 effect; in place of the single large effect of a tetanus lasting several minutes, we are in presence of a gradually developing and summating series of smaller effects of tetani lasting only $\frac{1}{8}$ minute at intervals of a minute.

Fig. 39. (958.)



Nerve 5 hours after excision giving a deflection of the second stage. Excitation once a minute for $\frac{1}{8}$ minute with coil at 10 units. Tetanisation for 5 minutes from α to ω.

Before the tetanus the successive negative variations increase slightly forming a "staircase." After the tetanus the negative variations are increased, gradually diminishing. An interruption (*int.*) of all excitation shows how the diminution was delayed by the excitation itself.

		Presumable Change of CO_2.
1	Deflection by 0·001 volt	
2	Normal series at minute intervals exhibiting staircase increase	Evolution in small quantities at each tetanus.
3	Tetanus lasting 5 minutes . . .	Evolution in considerable quantity by long tetanus.
4	Normal series	Dissipation of CO_2 evolved during previous tetanus, in spite of short tetani.
5	Interruption of series by 5 minutes rest	More rapid dissipation of CO_2 effect while the latter are intermitted.
6	Normal series	

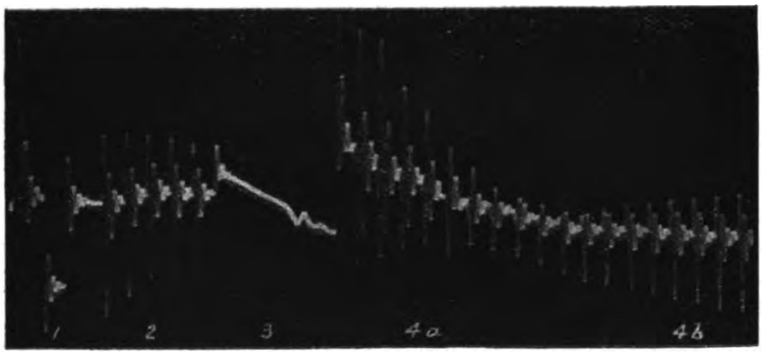
The regular effect of CO_2 is to increase the negative deflection of nerve in the first and second stages, and to diminish the positive variation of the third stage. The regular effect of tetani of $\frac{1}{8}$ minute at 1 minute intervals is to give series of slightly increasing negative deflections of nerve in the first stage, of markedly increasing negative deflections, and diminishing positive after-deflections of nerve in the second stage, and of diminishing positive deflections of nerve in the third stage (see fig. 31). In upwards of 500 observations available for study of that point no single exception is to be found to this rule, which is variously exemplified in all sorts and conditions of nerve. In the present communication it is best illustrated by the first portions of Obs. 958, fig. 39 (progressive increase of negative deflections of nerve in the second stage) of Obs. 858, fig. 31 (progressive diminution of positive deflections of nerve in the third stage), and of Obs. 2177, fig. 66.

Progressive Diminution of Positive After-Deflections of Nerve in the Second Stage.

Fig. 40 (Obs. 933) and fig. 41 (Obs. 843) are given in illustration of the temporary character of the reversal by tetanisation and by carbonic acid respectively. In the former case the reversal caused by 5 minutes tetanisation has disappeared in about 10 minutes; in the latter the reversal caused by a stream of CO_2 lasting for 5 minutes (*i.e.*, "much" CO_2) has endured for about 30 minutes.

Fig. 42 (Obs. 960) illustrates the great sensitiveness of nerve to tetanisation (and to CO_2) in the second stage; in this instance (which is one of the best marked of its

Fig. 40. (933.)



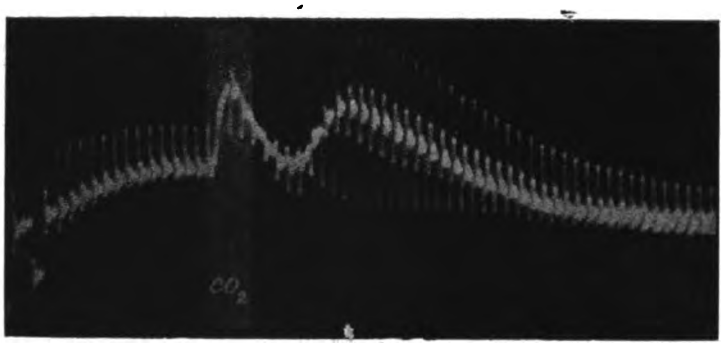
Nerve nine hours after excision, giving a deflection of the third stage, viz., N., temporarily reverted to S. in consequence of tetanisation.

1. Deflection by 0·001 volt.
2. Normal series N.S.
3. Tetanisation for 5 minutes.
4A. Normal series S.N., giving place to
4B. Normal series N.S.

This is one of the few instances in which a negative after-deflection has been observed; the nerve had been employed two hours previously to test upon it the effect of muscle-extract.

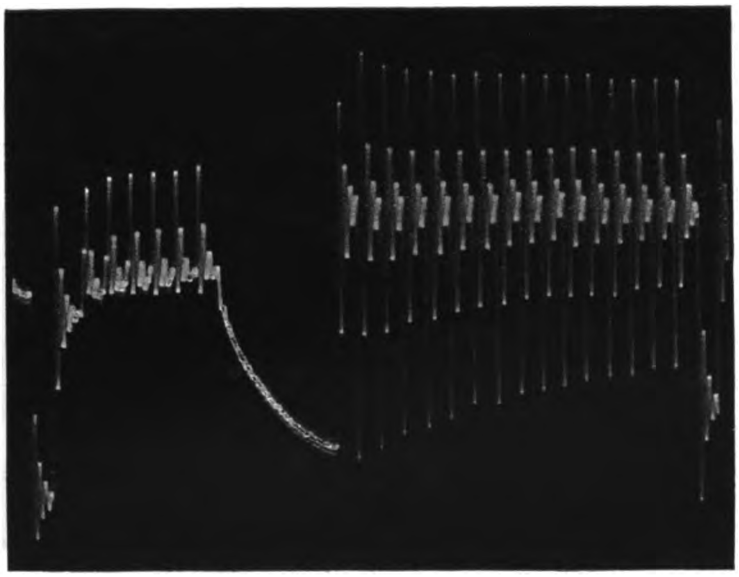
kind) the deflection before 5 minutes' tetanisation is barely visible, the after-deflection before tetanisation is markedly positive ; subsequent to the tetanisation the deflection is markedly negative.

Fig. 41. (843.)



Nerve 11 hours after excision, giving a deflection of the third stage, temporarily reversed, in consequence of CO_2 passed through the nerve-chamber for four minutes.

Fig. 42. (960.)



Nerve 10 hours after excision, giving a variation of the second stage (late) or third stage (early).

At the beginning of the record the deflection is *n*., and the after-deflection N. With successive excitations the *n*. deflection diminishes and disappears.

With the 5 minutes' tetanus (coil at 10 units) from α to ω, there is no α deflection, a rapidly increasing negativity from α to ω, and a large positive ω deflection. Subsequently the rhythmic excitation produces a large negative deflection gradually decreasing.

CHAPTER IV.—ON POSITIVE AND NEGATIVE EFFECTS OF EXCITATION.

§ 1. *State of the Question.*

The explanation nearest to hand of positive and negative variations and after-variations caused by excitation, is that which attributes opposite electrical concomitants to the opposite chemical movements of disintegration and reintegration of which all living matter is the seat.

A priori, every movement of disintegration must be made good by a simultaneous or subsequent movement of reintegration, and it was natural to suppose, with HERING and his pupils, that in medullated nerve we have a negative effect significant of the former, followed by a positive after-effect significant of the latter.

In nerve we have hitherto had no evidence of positive effects *during* excitation, other than phenomena that were attributable to the predominance of anelectrotonic currents aroused by the exciting current; at the present time the question of the physiological *versus* physical nature of such currents, their evidently close connection with the true negative variation or current of action, renders the whole problem especially intricate and obscure.*

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* Some of this obscurity is due to the varying import and theoretical connotations of the word "electrotonus." The term applies (1) to the permanent extra-polar currents aroused in a nerve that is traversed by a galvanic current; (2) to the similar, but much briefer, extra-polar currents aroused by induction shocks, and summing up to a steady effect when tetanising currents are used; and (3) to the brief propagated change giving rise to a current of action, and summing up to a "negative variation" of a demarcation current.

We may not sharply distinguish between an electrotonic current and a negative variation or action current; the better distinction to make is that between fixed and fugitive electrotonus, fixed electrotonus being a permanent phenomenon pervading the whole length of a nerve in diminishing degree with increasing distance from the polarising electrodes, fugitive electrotonus being a temporary phenomenon propagated along an undisturbed length of nerve in undiminished strength from the point at which a polarising current is suddenly altered. The current of action is a case of such fugitive katelectrotonus (HERMANN).

Permanent anelectrotonus (directed in the nerve towards the exciting electrodes) may be aroused by strong tetanising currents of whatever direction, owing to the normal superiority of the anelectrotonic over the katelectrotonic current, and therefore of the anelectrotonic sum over the katelectrotonic sum. Such anelectrotonus, as was pointed out by DU BOIS-REYMOND, in criticism of MOLESCHOTT ('MÜLLER'S Archiv,' 1861, p. 786, 1862, p. 241), will give rise to a pseudo-positive variation which is in no true antithesis to the negative variation. The latter is due to fugitive katelectrotonus, the former to permanent anelectrotonus.

The positive variation studied in this paper is produced by tetanising currents of minimal strength or little above, and the experimental argument in this chapter is in great measure directed to distinguish this positive variation as not being due to the fallacy of fixed anelectrotonus, but as being in true antithesis to the classical negative variation. To this end anæsthetics were used as described in the text. Anelectrotonus, as a coarse physical fallacy in DU BOIS-REYMOND'S sense, is excluded, without prejudice to the nature of the positive variation as a case of fugitive anelectrotonus (= A.), the opposite of the negative variation as a case of fugitive katelectronus (= K.).

Fugitive and permanent electrotonus cannot be sharply distinguished as physiological and physical

Electrotonic currents are clearly the effect of core-polarisation (HERMANN); they are reproducible on polarisable core-models, and in this sense "physical," but they are far better shown on "living" than on "dead" nerve, and in this sense they are physiological. They cannot be sharply distinguished into physical and physiological components. Nor is it possible to draw any sharp line of distinction between a negative variation and an electrotonic current; the former, like the latter, can be reproduced on a core-model (BORUTTAU), and must be regarded as an instance of propagated temporary katelectrotonus.

At the outset of these observations, I sought to distinguish the true negative variation due to a fugitive state of katelectrotonus from the fallacy of the permanent or fixed electrotonic state associated with steady electrolytic polarisation and spread of current. The negative variation provoked by tetanising currents alternating in direction, was found to be independent of that direction, and subject to the influence of anæsthetic and other sedative drugs in an unmistakably physiological manner. This negative variation, subsequently the positive after-variation, and finally the positive variation, were found to be on a similar footing, physiologically modifiable by drugs. The most questionable of these phenomena, the positive variation, which might obviously be due to predominant anelectrotonus caused by alternating currents whatever their direction, was found to be particularly sensitive to the action of reagents, and could therefore not be classed as a fallacy due to exclusively physical polarisation. It must, I think, be admitted to rank as a true action current on the same terms as the negative variation, and, if the latter is propagated katelectrotonus, the former is propagated anelectrotonus. Whether the appearance of one or other of these phenomena is dependent upon the different rate of development of the two states under different conditions, and the consequent predominance of one or other sum of effects under the influence of a given series of induction shocks, is a question into which I cannot now enter. The simple and obvious statement in terms of HERING'S theory (negative variation a sign of dissimilation, positive variation a sign of assimilation) is extremely convenient as a description, but is not finally justified until we are more fully acquainted with the electrolytic changes occurring in the polarisation of living nerve. And although I shall tentatively describe certain facts n terms of that theory, it can only be with the express reservation that the physico-chemical mechanism of anodic and kathodic polarisation may or may not prove to harmonize with such a mode of description. Yet, whether the theory fits the facts or not—whether, *e.g.*, the positive variation be or be not a token of integrative

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by means of anæsthetics; they are presumably closely related phenomena of which the electrolytic polarisability of nerve is the common condition, the former requiring a nerve of greater instability than the latter.

In order to escape as far as possible from ambiguity in the use of the terms, the initial letters A. and K. are occasionally (*e.g.*, on p. 64) used to denote fugitive electrotonus, while the full words anelectrotonus and katelectrotonus are used only to designate permanent electrotonus (*e.g.*, on p. 58).

movement, and the anode the pole by which rest, inhibition, and "assimilation" are evoked, in contrast with the kathode evoking action, excitation, and "dissimilation"; or whether, *e.g.*, the conversion of a positive into a negative variation under the influence of carbon dioxide or of prolonged tetanisation be due to altered time-relations of anelectrotonic and katelectrotonic effects—the facts will remain, and doubtless contribute to the future elucidation of this obscure corner in electro-physiology. I think it quite possible that facts which can be most obviously exposed in terms of **Hering**'s theory of antagonism, may be more accurately described in terms of **Hermann**'s theory of electrotonus, yet that in the end the two sets of terms may be found to denote the same opposed chemico-physical changes in living matter.

Meanwhile it is desirable that I should, as briefly as possible, describe the experiments I have so far been able to make in this direction, and the theoretical interpretation of which they appear to be susceptible.

To this end it will be convenient to give (1) a more connected account of experiments already touched upon in Chapter III., concerning the effects of tetanisation; (2) a preliminary account of experiments concerning the action of carbon dioxide on polarisation phenomena; and (3) what seem to be the principal hypothetical inferences based upon these various data.

§ 2. *Effects and After-Effects of "Brief" Tetanisation.*

The ordinary deflection of normal fresh or nearly fresh nerve during tetanic excitation is, as was discovered and determined by **du Bois-Reymond**, negative to the current of injury. This "negative variation," as was first pointed out by **Hering**, is frequently followed by a "positive after-variation" (viz., in the same direction as the current of injury) smaller than the preceding negative variation.

In conformity with the plan of connections (fig. 3) observed throughout these observations, this normal galvanometric response *during* and *after* excitation is to be designated by the symbol S.n.

A nerve left to itself in normal saline—(for 1 to 2 hours in summer, for 6 to 12 hours in autumn) will, in all probability, exhibit a response of similar type, in which, however, the positive after-variation is larger than the preceding negative variation, to be designated, therefore, by the symbol s.N.

				Deflection.	After deflection.
1.	Large negative,	followed by	small positive	S.	n.
2.	Small negative	,,	large positive	s.	N.
3.	Nil	,,	positive	0	N.
4.	Positive	,,	positive	N.	N.
5.	Positive	,,	negative	N.	S.
6.	Negative	,,	negative	S.	s.
7.	Nil, or small negative	,,	negative or large negative	0 or s.	S. S.

Later still, especially in summer, or in winter after the nerve has been under prolonged experiment of various sorts, the variation *during*, as well as after, excitation, may be observed to be positive.

It has been convenient to take these three points as being respectively characteristic of three states or stages :—

1st stage, "fresh." Negative deflection larger than positive after deflection, S.n.
2nd stage, "transitional." Negative deflection smaller than positive after deflection, s.N.
3rd stage, "stale." Positive deflection, N.

In the third stage, of which the positive deflection is taken as the characteristic, the after-deflection may be positive (usually) or negative (exceptionally), and, in addition to the responses formulated above, I have observed cases of a negative deflection followed by a negative after-deflection, and of no deflection followed by a positive after-deflection.

The *à priori* conceivable list of possible varieties of response (omitting as of uncertain determination cases of zero after-deflection) is now complete, with one significant exception, which is indicated in parentheses, and has never come under my observation.

Of the above list, the first four members include the types of response that have most frequently come under my observation; they form a sequence, in so far as two or more members may always be observed to follow each other in the order named, from 1 to 4, and may always be made to follow each other backwards from 4 to 1 by the chief disintegration product CO_2 (A) externally applied to the nerve, and (B) presumably evolved from within the nerve itself during a prolonged tetanisation. This reversal of sequence has, in fact, been fully described in Chapter III., where the sequence itself, now to be considered, was unavoidably stated in dogmatic form in preface to a detailed description of its reversal by CO_2. It may, however, be mentioned that a similar reversal is effected by various other means—by formic and lactic acids, *e.g.*, and by a renewed transverse section.

The fifth member of the list, viz., a positive deflection followed by a negative after deflection, N.S., was far less frequently and assuredly observed, and I do not know whether, in order of development, it should be placed before or after the response N.N. The after-effect S. is, in this case, never very pronounced, so that, in view of the uncertainty of instrumental correction considered in the head-note to Table D, it may have been present in slight degree more often than it was obviously present.

The sixth member, viz., persistence of a negative effect as negative after-effect, was also infrequently observed otherwise than as a consequence of CO_2 (when it was practically constant for nerve in the 2nd stage), or of strong stimulation (when it may in part have been a CO_2 effect), or of chemical modification. This infrequency was somewhat surprising in view of the experience of previous observers (HERING among others), who have noted a depression of current subsequent to the usual negative variation during excitation. I have, indeed, observed such a depression as a regular consequence of strong excitation, but a negative after-effect concentrated enough in time to give an impulse to the mirror of my galvanometers has been comparatively rare. And, as will be shown in connection with the terminal deflection of prolonged tetanisation, negative after-swing is then comparatively rare and only met with in some cases of nerve in the 3rd stage; in the other stages the terminal deflection has always been positive, as well as in most instances of nerve in the 3rd stage under the conditions of my experiments. An immediate negative after-effect of a negative effect must then be exceptional and restricted to certain special conditions of strength and time of tetanisation; prolonged negative after-effect, on the other hand, is a practically constant phenomenon. Positive after-effect following upon positive effect has been as common, as negative after-effect following upon negative effect has been rare.

The seventh member (or pair of members), viz., a negative after-effect larger than a previous negative effect—s.S. or 0S.—has never come under my observation. The opposite case of a positive effect followed by a larger positive after-effect—n.N., or actually 0N.—has been very common.

The possible cases, S.0, N.0, have not been included in the above list for the reason that, though they have both no doubt occurred, the instrumental correction necessary in the case of after-deflection forbids us to conclude to perfect absence of after-effect. Cases occurred, indeed, in which it was calculated as being absent, but in which we may with safety only draw the conclusion "little or none." This is, however, as regards the surveys before us, a comparatively immaterial and purely formal drawback. We may, as the case arises, draw the far more essential conclusion that an after-effect has become more positive or more negative, and plot out a curve of modified after-effects nearly (but not quite) as strictly justified as a curve of modified effects.

The members most essential to our experimental and theoretical study have been the first four, viz., S.n., s.N., 0N., and N.N., which—considering the experimentally somewhat striking case of 0N. as a case of s.N. with vanishing s.—are reduced to three, which are taken as the basis for classifying the states of nerve as first, second, and third. Of these three members the first and third, in which the currents during excitation are respectively negative and positive, are the principal contrasting types. The intermediate type, in which the current after excitation is prominently positive, is preserved as a separate class, partly because it is representative of a very usual condition of experiment, partly because it is the bridge between the two principal extremes.

§ 3. *Effects and After-Effects of "Prolonged" Tetanisation.*

The effects and after-effects hitherto described have been such as are produced by brief tetanisation, lasting 7·5 seconds. We have now to review the effects and after-effects produced by prolonged tetanisation, lasting 5 minutes, such as was used to test the nerve for CO_2 effects, as described in the previous chapter. And in this review we shall find it convenient to follow the classification made above of three states of nerve—fresh, transitional, and stale.

Fig. 43. (Plate 2148.)

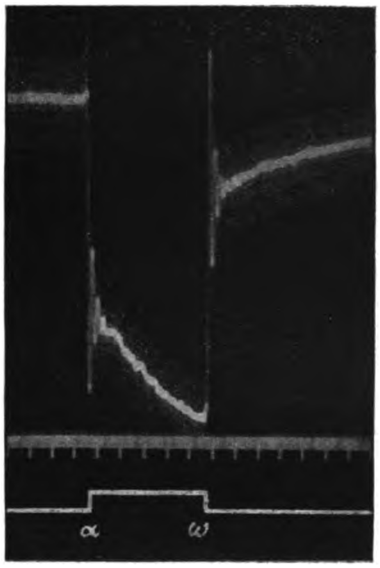


Fig. 44. (Plate 936.)

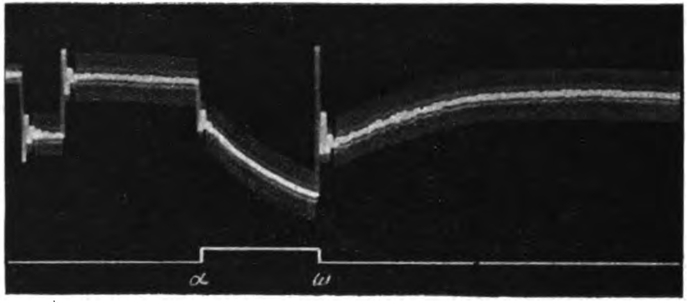
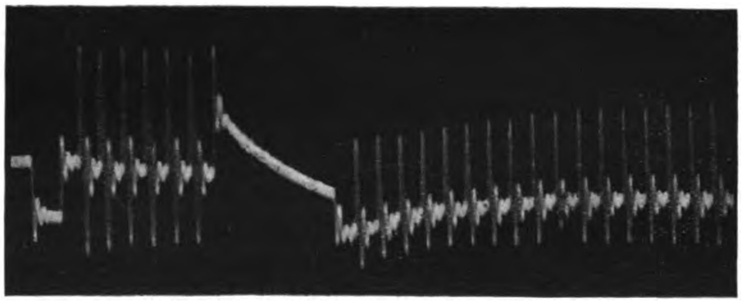


Fig. 43.—February 3, 1896.—Nerve a few minutes after excision, giving a variation of the first stage. Tetanisation for 5 minutes from α to ω; coil at 10 units.

Fig. 44.—December 10, 1895.—Nerve 10 hours after excision, giving a variation of the second stage. Tetanisation for 5 minutes from α to ω; coil at 10 units.

Fig. 45. (874.)

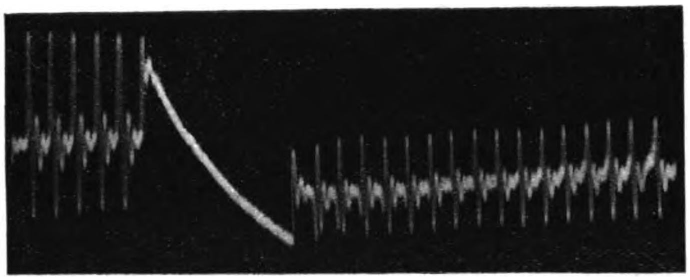


November 30, 1895.—Nerve 10 hours after excision (previously used for observations with ether and with CO_2), giving a variation of the 3rd stage (positive), with a negative ω deflection at the end of 5 minutes' tetanisation, and a diminution of the positive effect of excitation. ("Disguised" effect.)

With nerve in the first and second stages, the alterations of current during and after tetanisation are in accordance with figs. 43 and 44, in which the duration of tetanus is marked from α to ω, α being its initial, ω its terminal, deflection. The α deflection is S. or negative; the course of steady deflection is southward or increasingly negative; the ω deflection is N. or positive; the subsequent state of current is negative to the state before tetanisation, and gradually becomes less negative.

The curve of increasing negativity during tetanus falls convex to its abscissa, viz., by a diminishing increment, being not far from logarithmic (*e.g.*, figs. 39 and 42); the curve of decreasing negativity after tetanus rises convex to its abscissa by a diminishing decrement (*e.g.*, figs. 44 and 45).

Fig. 46. (898.)



December 5, 1895.—Nerve several (?) hours after excision (previously used for observations with sarcosin), giving a variation of the 3rd stage, with a positive ω deflection at the end of 5 minutes' tetanisation, and a reversal of the effect of excitation. ("Clear" effect.)

With nerve in the second stage giving the deflection 0N., there is little or no α deflection, and a large positive ω deflection, the current during tetanisation consisting in a gradually increasing negativity (fig. 42).

With nerve in the third state, the α deflection is N. or positive; the course of steady deflection during tetanisation is southwards or diminishingly positive (or increasingly negative); the ω deflection is either negative or positive; the subsequent state of current is negative to the state before tetanisation, and gradually becomes less negative. It was according to the character of the ω deflection that two varieties of third stage effect were distinguished in Chapter III., (*a*) that in which the ω deflection was N. or positive, and the effect of CO_2 "disguised" (diminution of N.); (*b*) that in which the ω deflection was S. or negative, and the effect of CO_2 "clear" (replacement of N. by S.) (figs. 45 and 46).

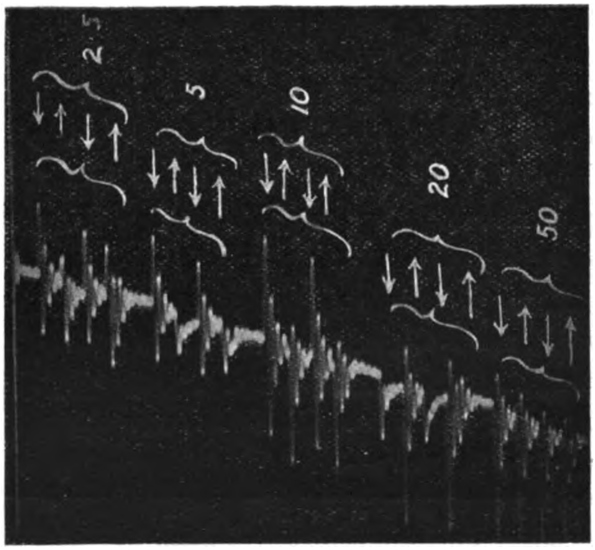
The points of identity and of difference in the tetanic alterations of the three stages may now be summarised as follows :—

State.	Effect before tetanus.	α.	During tetanus.	ω.	Effect after tetanus.
1st	S.	S.	Sward	N.	Increased S.
2nd	s. or 0	s. or 0	Sward	N.	Increased S.
3rd, *a*	N.	N.	Sward	N.	S.
b	N.	N.	Sward	S.	Diminished N.

It will naturally be asked what significance belongs to these facts; what is their dependence, if any, upon the strength and length of excitation in relation to state of nerve, and whether there is any significant relation to be traced between an α and an ω deflection under various conditions, &c., &c. All these questions are difficult to answer; the general question of significance will be considered by itself, other questions of fact, to which owing to the number of variables I can only give incomplete or fragmentary answers, may receive such answer at this stage. But, whereas the more general statements heretofore made are presented as generalizations resting upon a number of particular experiments considered as affording a broad enough basis, the following are to be regarded almost in the light of particular observations, which a more extended survey may (or may not) demonstrate to be representative of general relations. Separate investigations of considerable extent will be required before this conclusion may safely be arrived at.

Strength of Excitation.—I have observed more than once (but am unable to reproduce the experiment at will) that nerve in the 3rd stage giving with weak tetanisation the deflection N., gives with stronger tetanisation the deflection S. The following is a case in point (826), which is reproduced in fig. 47, partly in order to give an example of how such measurements are made, partly because a critic may see in it internal evidence of some possible explanation or fallacy that I am unable to detect. The facts here signify possibly that the nerve has been in such a state that fixed anelectrotonus was manifested at lower current strength than fugitive katelectrotonus. This possibility of a fixed anelectrotonic component is further supported

Fig. 47. (826.)



by Obs. 2149,* where, with constant strength but diminishing interpolar distance, the negative variation was diminished, viz., at 15 millims. it was — 17, at 10 millims. it was — 8, at 5 millims. it was 0.

Strength.	Deflection (descending break).	Deflection (ascending break).
2·5 units	N. 9·5	N. 3·5
	N. 9	N. 7
5 „	N. 9	S. 5
	N. 8·5	S. 6·5
10 „	N. 13·5	S. 14·5
	N. 13	S. 12
20 „	S. 9	S. 18
	S. 7	S. 18
50 „	S. off plate	S. off plate
	S. off plate	S. off plate

The galvanographic curve of a prolonged tetanic variation is extremely like that of an ordinary muscular tetanus, both as regards the gradual tetanic increase and the

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* December 1, 1896.—Obs. 2149 was somewhat exceptional; other observations, of a presumably more typical character, made for the purpose of comparing the effects of tetanisation with assuredly electrotonic effects, showed no difference of the negative variation with different distances between exciting and leading-off electrodes, *e.g.*:—

OBS. 2107.—Leading-in electrodes, 1 centim. apart. Leading-out electrodes, ditto.

Length of nerve between leading-in and leading-out electrodes.	Anelectrotonic current by 1·4 volt.	Katelectrotonic current by 1·4 volt.	Negative variation by tetanisation at 15 units, in both directions; 66 interruptions per sec. for 7·5 secs.	
centims.				
3	+ 1·5	— 0·5	—3·5	—4·0
2	+ 7·5	— 2·5	—4·0	—4·0
1	+120·0	—90·0	—4·0	—4·5

December 5, 1896.—Exp. 2131. Nerve giving a deflection of the third stage. Intrapolar distances = 1 centim. each; polarising current by 1 Leclanché; 0·001 volt gives 13 millims. deflection.

Length of nerve between leading-in and leading-out electrodes.	Anelectrotonic current.	Katelectrotonic current.	Positive variation by tetanisation at 15 units, in both directions for 7·5 secs.; 66 interruptions per sec.	
centims.	millims.			
3	+ 0·5	Trace	+8·5	+8·0
2	+ 2·0	— 1·0	+8·0	+8·0
1	+34·0	—23·0	+8·0	+8·0

gradually diminishing after-tetanic remainder. In nerve, at least, the effect is attributable to CO_2 gradually evolved during the tetanisation, gradually dissipating itself (or, perhaps, "reinvolved") after tetanisation. Owing to the gradual increase of the negative deflection during tetanus, it always happens in the first, and still more markedly in the second state of nerve, that the ω positive swing is greater than the α negative swing. (I did not, of course, neglect to verify the equality of the two opposed swings caused at make and break of a prolonged constant current; proof of this equality is, indeed, afforded by the standard deflection of $\frac{1}{1000}$ volt, taken at the beginning and end of most of the observations, *e.g.*, the standard deflection at the end of fig. 42.) With nerve in the 3rd stage, in which the α deflection is positive, the ω swing may be greater, equal to, or smaller than the α swing; it may be positive, negative, or so small as to be of doubtful direction. It is negative and smaller than the α deflection if, during tetanisation, the positive state has only diminished. It is positive and either smaller or larger than the α deflection if, during tetanisation, the positive has given place to a negative state. A negative ω deflection smaller than the corresponding positive α deflection is present in figs. 32 and 45; a positive ω deflection smaller than the corresponding positive α deflection is present in fig. 46; a positive ω deflection larger than the corresponding positive α deflection is present in figs. 31 and 46.

There is, as might be expected, a fairly regular relation between the difference of the α and ω swings and the deflections of the minute before and minute after tetanus. This relation is most regular in the 1st and 2nd stages, where the two differences are greater and smaller together.

	$\omega-\alpha$.		d_2-d_1.*
E.g., in 741 (fig. 29) the two differences are respectively . .	15	and	7
,, in 689 the two differences are respectively	18	,,	8
,, in 761 ,, ,, ,, ...	7	,,	4
,, in 876 ,, ,, ,, ...	4·5	,,	2·5
,, in 960 (fig. 42) the two differences are respectively . .	45·5	,,	34

Other instances are contained in Table D.

The relation is not so clear nor so constant in the third stage, where the α deflection is + and the ω deflection + or −. With a positive ω it generally happens that the larger the ω the larger the succeeding negative deflection, *i.e.*, the greater the difference between that deflection and the deflection immediately preceding the tetanus.

E.g., in 933 (fig. 40) $d_1 = +\ 6{\cdot}5,\ \alpha = +\ 6{\cdot}5,\ \omega = +\ 30,\ d_2 = -\ 15{\cdot}5,$

,, in 898 (fig. 46) $d_1 = +\ 13,\ \alpha = +\ 13,\ \omega = +\ 12,\ d_2 = -\ 6.$

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* d_1 signifies the last ordinary deflection preceding tetanisation, d_2 the first ordinary deflection subsequent to tetanisation.

With a negative ω, it generally happens that with larger and smaller ω are associated smaller and larger diminution of an original deflection.

E.g., in 874 (fig. 45) $d_1 = +17$, $\alpha = +17$, $\omega = -7\cdot5$, $d_2 = +12$,
„ in 782 $d_1 = +11$, $\alpha = +11$, $\omega = -11$, $d_2 = +11$,
„ in 942 $d_1 = +11$, $\alpha = +11$, $\omega = -23\cdot5$, $d_2 = +13\cdot5$.

These last three examples are chosen to illustrate the, for the moment, empirical relation between the two differences, and include what have been referred to as exceptional effects of tetanus (viz., augmentation of a north, diminution of a south deflection). As may be noticed in the three cases, with a negative ω smaller, equal to, and larger than the corresponding positive α, we have a positive d_2 smaller, equal to, and larger than the corresponding positive d_1.

§ 4. *Preliminary Account of the Action of* CO_2 *upon Polarising and Electrotonic Currents. Polarisation Increments and Electrotonic Decrements.*

Experiments under this head were undertaken principally with the object of determining whether or no the positive variation upon which I had studied the action of reagents was a phenomenon of ordinary fixed anelectrotonus or a fugitive effect, the counterpart of the negative variation. They were commenced on the inadequate supposition that ordinary electrotonic effects, being reproducible on the core-model, are physical phenomena independent of the physiological state of nerve, and should therefore be refractory to the action of anæsthetics. On this supposition anæsthetics should have furnished the distinction between electrotonic (physical) and excitatory (physiological) effects, and the positive variation would at once have been placed in one or other category.

The effects of anæsthetics (carbon dioxide, ether, chloroform) were studied upon :—

1. Polarising currents; 2. the excitatory increments of polarising current; 3. electrotonic currents; 4. the excitatory decrements of electrotonic currents, and although the simple distinction just alluded to could not be absolutely established, certain results were obtained calculated to further our comprehension of electrotonic effects and indirectly to establish the positive variation as a physiological phenomenon on the same footing as the negative variation.

Detailed description of these experiments will be given on a future occasion; at this juncture only the briefest possible summary of results is presented, in so far as these are connected with the influence of carbon dioxide upon the polarisation phenomena of which the electrical effects of excitation are a special case.* The diagram (fig. 48) enumerating the several currents that have been tested by anæsthetics, and the eight plates (figs. 49 to 56) giving typical results of the action of carbon dioxide, will most clearly and briefly fulfil this purpose.

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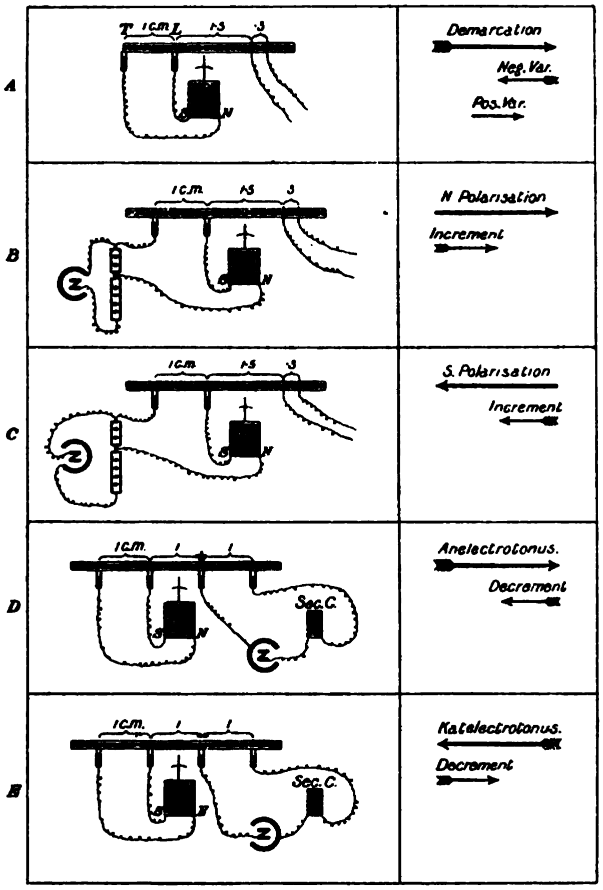
* BORUTTAU's recent demonstration (PFLÜGER's 'Archiv,' vol. 58, p. 1, 1894, and vol. 63, p. 145, 1896), on core-models of platinum in saline solution, of a wave of negativity provoked by tetanisation, travelling with measurable velocity (150 to 170 metres per second) and not very marked decrement, thus giving rise to a typical diphasic variation, has very completely fulfilled the identification of the electrical phenomena in excited nerve with polarisation phenomena, in accordance with HERMANN's point of view.

Fig. 48



Plan of the several currents referred to in the text and recorded in the next group of 8 plates.

The connections are such that in each case the direction of the arrow indicates the direction of current in the nerve and in the galvanometer.

Current in the nerve from left to right is indicated by current in the galvanometer from S. to N. ("positive"), reading upwards on the final record; and *vice versâ.*

For electrotonic currents and their excitatory decrements the polarising and exciting circuits were conjoined, and completed through the nerve by the same pair of unpolarisable electrodes.

Anæsthetics (represented in the figures by CO_2)* produce no effect upon the strength of polarising currents, but, as was to be expected, polarisation increments and electrotonic decrements, which are essentially action-currents, are modified by

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* Instances of the action of Et_2O and of $CHCl_3$ are given in a paper dealing more especially with the question of anæsthetics in current numbers of 'Brain' (1896). Some experiments are quoted in Table E, and the subject will be dealt with more fully in a future paper. As regards carbon dioxide the influence of quantity, and the effects of tetanisation will be there considered.

CO_2, and ordinary electrotonic currents, contrary to expectation, although apparently less sensitive, are distinctly altered.

We cannot, therefore, sharply distinguish between an ordinary electrotonic and an action-current by means of anæsthetics, even though we may have found that the latter is more easily affected than the former. Electrotonus is a physical phenomenon inasmuch as it occurs on any polarisable core model, and, in such case, it is not affected by anæsthetics. But it is also a physiological phenomenon, inasmuch as the chemical instability, viz., polarisability, characteristic of the living nerve (and no doubt in less degree retained by nerve that is called "dead") is essential to its manifestation. If the nerve is temporarily fixed by an anæsthetic, or permanently fixed by a poison, *e.g.*, by aconitine, the polarisability and depolarisability that are essential to the manifestation of electrotonic phenomena no longer exist, and the nerve loses, first its capability of undergoing the transmitted and temporary effect ("fugitive electrotonus"), next its capability of undergoing the permanent effect ("fixed electrotonus").

This conclusion seems to be not entirely in harmony with BIEDERMANN'S results,* partly, perhaps, by reason of different senses attaching to the term electrotonus, partly, perhaps, by reason of differences in the conditions of experiment.

BIEDERMANN distinguishes in the extra-polar current produced during and after the passage of a constant current (1 to 3 volts, 10 millims. between polarising and galvanometer electrodes) a physiological factor dependent on propagated excitation in the living nerve and a physical factor dependent upon its anatomical integrity. The former "physiological electrotonus") he finds to be subject to *temporary* suppression by "brief" (5 to 10 minutes) etherisation. The latter ("physical electrotonus") he finds to be relatively more stable, but to undergo diminution and *definitive* abolition by further "prolonged" etherisation destructive of the nerve. Current that is temporarily suppressed by etherisation is regarded by BIEDERMANN as an expression of physiological electrotonus; the residual current, that can only be suppressed, and then finally so, by "prolonged" etherisation, he considers as being due to physical electrotonus.

I find that electrotonic as well as action currents (otherwise expressed permanent as well as fugitive electrotonus) may be *temporarily* suppressed by anæsthetics. And whereas BIEDERMANN from his observations adopts anæsthetics as distinguishing between physiological and physical electrotonus, I from mine do not feel entitled to make any sharp distinction by such means between the ordinary electrotonic and the true action current. Both have been sensitive although unequally so, and, much as I desired to draw the line between electrotonus and action-current, I did not feel it safe to do so by means of anæsthetics, which in my hands have served rather to draw the line between electrotonus and current diffusion.† The latter is especially liable to

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* 'Electrophysiologie,' vol. 2, p. 695, Jena, 1895.

† I have Professor HERING'S authority for stating that the term "physical electrotonus" arose in his laboratory as an expression denoting neither more nor less than "current-diffusion." (Leipzig, Dec. 22, 1896.)

Fig. 49.

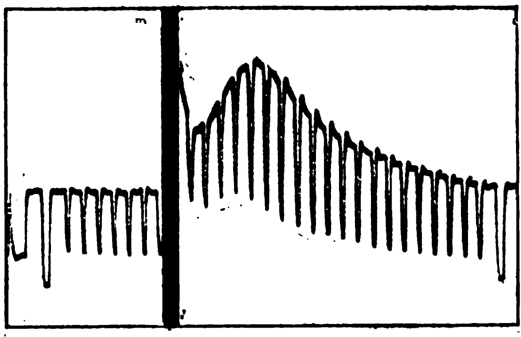


Fig. 50.

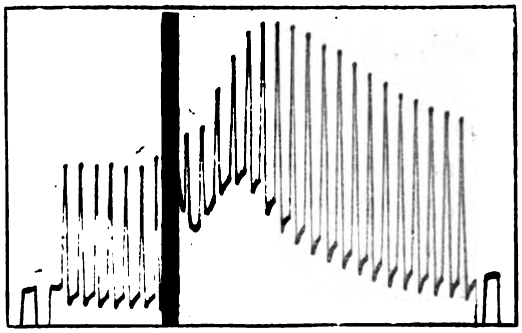


Fig. 51.

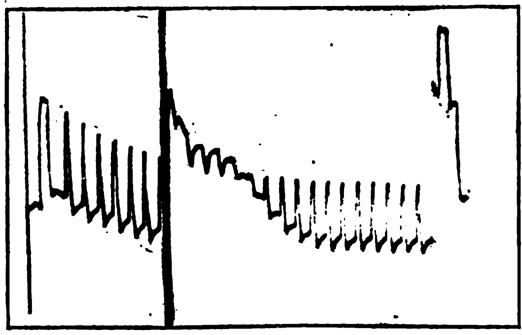


Fig. 52.

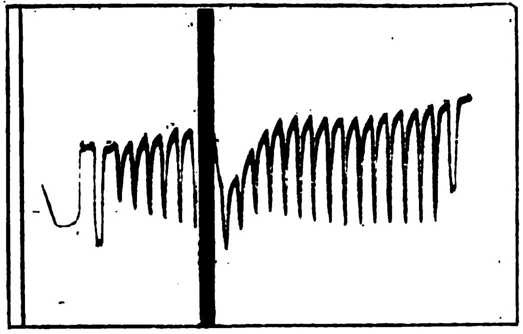


Fig. 53.

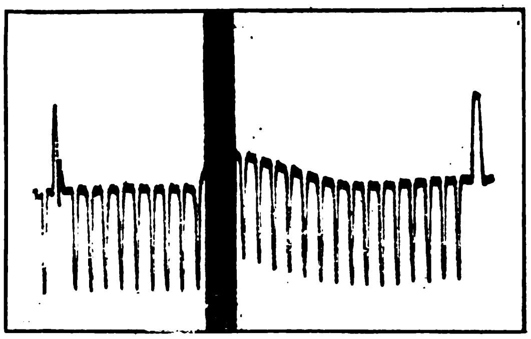


Fig. 54.

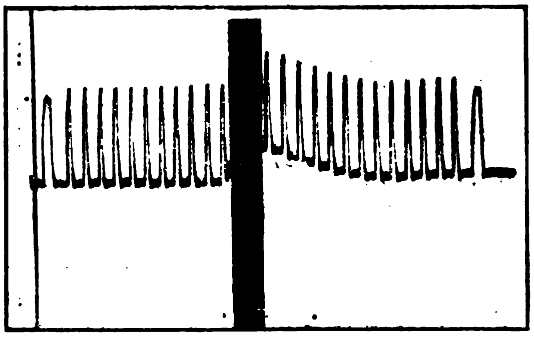


Fig. 55.

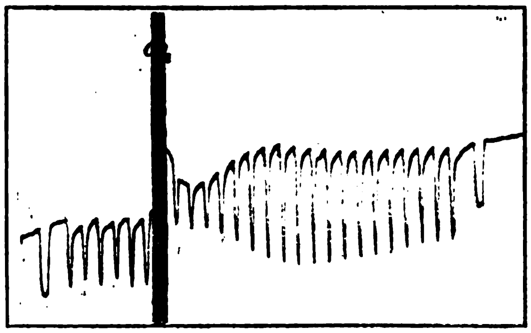


Fig. 56.

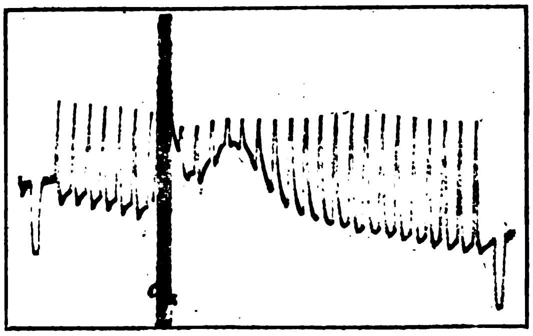


Fig.	Plate.		Fig.	Plate.	
49	2195	Effect of CO_2 on katelectrotonus	50	2199	Effect of CO_2 on anelectrotonus
51	2181	" " a katelectrotonic decrement	52	2185	" " an anelectrotonic decrement
53	2207	" " a S. polarising current	54	2208	" " a N. polarising current
55	2204	" " a S. polarisation increment	56	2203	" " a N. polarisation increment

The above eight records were taken by the dead-beat galvanometer, with connections as indicated in fig. 48.

In the observations on katelectrotonus and anelectrotonus (figs. 49 and 50), the polarising current was by one Leclanché cell (= 1·4 volt) with distances (*a*) between polarising electrodes, (*b*) between polarising and galvanometer electrodes, (*c*) between galvanometer electrodes, each = 10 millims. An interrupter (make = 15 secs., interval = 45 secs.), was placed in the polarising circuit.

In the observations on the two electrotonic decrements (figs. 51 and 52), the polarising and exciting currents entered the nerve by the same pair of unpolarisable electrodes (figs. 48D and 48E), the interrupter was in the exciting circuit.

In observations on the polarisation increment (figs. 55 and 56), the polarising current was taken = 0·05 volt. (figs. 48B and 48C). The interrupter was in the exciting circuit.

occur in such experiments, where a comparatively high electromotive force (over 1 volt) is turned on at intervals. When, in consequence of an anæsthetic or toxic drug, an originally unequal anelectrotonus and katelectrotonus has given place to a reduced effect equal in the two opposite directions, the latter has in some instances disappeared after the nerve has been completely crushed in the interpolar region, while in other instances it has persisted little if at all diminished, *i.e.*, in some instances (Table E, Obs.) the residual deflection has been attributable to BIEDERMANN'S "physical electrotonus," in others it has clearly been due to current escape. But the point is one requiring further study; as regards the present investigation, it is a side-issue.

With regard to a positive variation, it might possibly be due to—

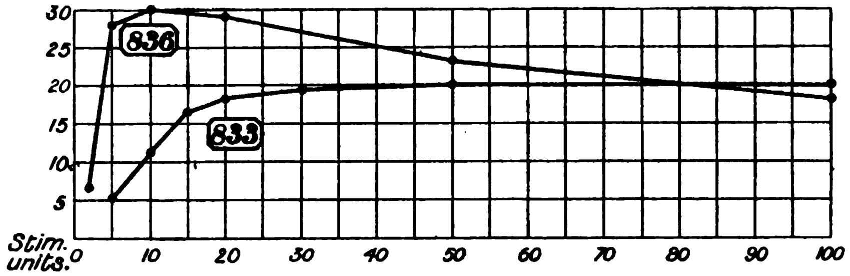
(1). An ordinary anelectrotonic current.
(2). A negative variation of an ordinary katelectrotonic current.
(3). A north polarisation decrement.
(4). A fugitive anelectrotonic current.
(5). Current escape.

The possibilities (2) and (3) may be dismissed at once; the positive variation cannot be a negative variation of a katelectrotonic current in the absence of katelectrotonus, nor a polarisation increment in the absence of a polarising current. And the fifth alternative, which certainly might, and does appear with an imperfectly insulating moist chamber, besides being excluded by the usual test of crushing in the interpolar region, is further dismissed by the temporary action of CO_2 and other anæsthetics. We are thus left in presence of the alternatives (1) and (4).

The positive variation is produced by very weak currents, and *sometimes* is lost when the current is strengthened. It is extraordinarily sensitive to reagents, especially to a presumably infinitesimal amount of carbon dioxide which leads to its diminution or reversal. Like the negative variation, but unlike an ordinary anelectrotonic current, it does not depend upon the distance between the leading-in and the leading-out electrodes. Confirmatory evidence is, I think, afforded by the absolute identity in the effects of carbon dioxide (and other reagents) upon a positive after-deflection and a positive deflection. The former (HERING'S positive 'Nachschwankung'), is a state of predominantly positive reaction consequent upon a previous state of predominantly negative action, interpretable as a physiologico-chemical assimilation consequent upon previous dissimilation. Or, in electrotonic language, it is an anti-katelectrotonic (fugitive) after-effect. If so, and if the positive after-deflection is of the same genus as the positive deflection, then the interpretation good for the former is good also for the latter.

In the case of the negative effect, the range from minimal to maximal is extensive, and the maximal effect is, as a rule, gradually and indefinitely increasing. In that of the positive variation, the range from minimal to maximal is narrow; in general rule a positive maximum has been reached with a strength of tetanisation not greatly in excess of the minimal effective, and has undergone more or less pronounced diminution with further increased strength of tetanisation; in a few instances (*e.g.*, fig. 47), with such increase, a positive has given place to a negative deflection. If the positive variation were due to ordinary anelectrotonus, these relations should be reversed; the positive variation should increase indefinitely, and a negative variation at lower stimulation-strength should have given place to a positive variation at higher stimulation-strength. This I have never witnessed.

Fig. 57.

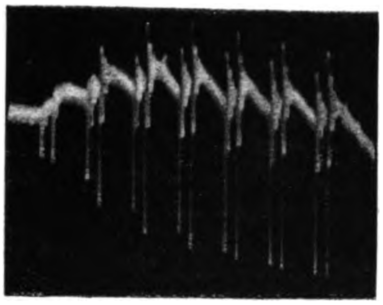


	Strength of stimulation.	Magnitude of deflection.	Value of 0·001 volt.	
833	units.	millims.	millims.	Break desc.
	5	− 5·5	48	
	10	− 11		
	15	− 16·5		
	20	− 18		
	30	− 19·5		
	50	− 20		
	100	− 20		
836	1	+ 0	22	Break desc.
	2	+ 6·5		
	5	+ 28		
	10	+ 30		
	20	+ 29		
	50	+ 23		
	100	+ 18	22	

Observations 833 and 836 (figs. 58, 59), illustrate this point, especially if their respective measurements are plotted out as curves (fig. 57). The former gives the series of increasing negative variations of a nerve of the 1st state, the latter, the series of diminishing positive variations of a nerve of the third state.

The positive after-effect of the second state of nerve undergoes a similar decrease with increasing strength of stimulation, as may be anticipated from its regular decrease, with series of brief tetanisations of constant strength. Whereas, as previously stated, the negative effect of such nerve undergoes staircase increase, its positive effect undergoes staircase decrease, phenomena that are attributable to an evolution of carbon dioxide, and the second of which further bears out the identity in kind between the positive effect and the positive after-effect. This point, incidentally present in several other figures of this paper, *e.g.*, in fig. 66, is more particularly illustrated by the plotted curves of fig. 60, with which are given the actual records from which this figure is derived (figs. 61 and 62).

Figs. 58, 59 (Plates 833, 836).



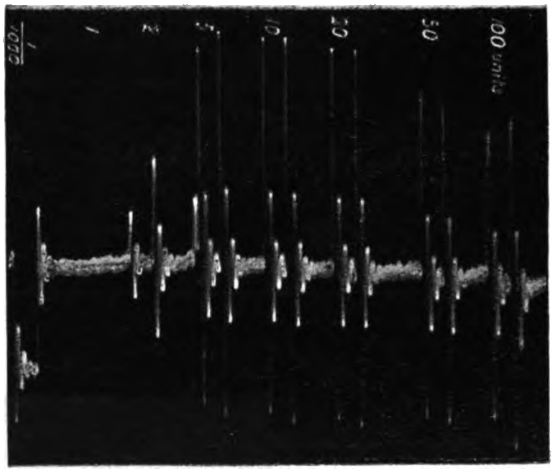


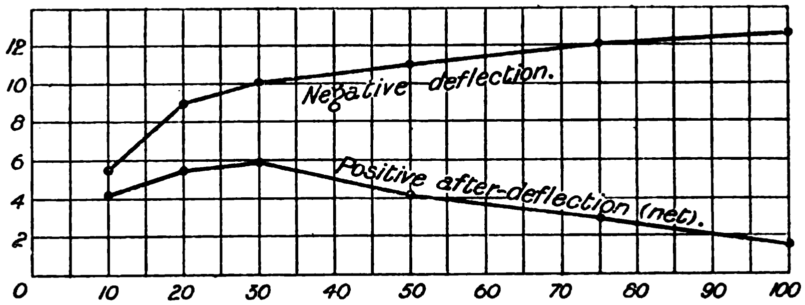
Fig. 58.—Records from which the measurements were taken for the construction of the curves of fig. 57.

Fig. 59.—Excitations in pairs, first with break descending, *i.e.*, towards the galvanometer electrodes, then with break ascending. Only the former have been used for the construction of the curves.

Finally, we may comment upon a point already mentioned at an earlier stage, viz., the rarity of a negative as compared with a positive after-effect; it has most commonly happened that a positive after-deflection has taken place succeeding not merely a negative but also a positive deflection; if the positive deflection had been due to ordinary anelectrotonus it should have been followed by a negative after-deflection.

The weight of evidence is thus against the ordinary anelectrotonic nature of the positive variation produced during tetanisation, and towards its recognition as an excitatory phenomenon, similar to the positive after-variation, and the counterpart of the negative variation.

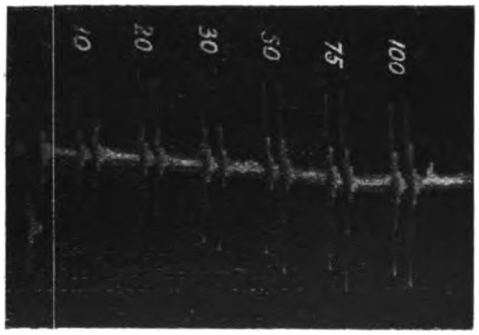
Fig. 60.



2070

Strength of stimulation.	Magnitude of negative deflection.	Magnitude of positive after-deflection.*
10	− 5·5	+4·3
20	− 9	+5·5
30	−10	+5·8
50	−11	+4·2
75	−12	+3·0
100	−12·5	+1·7

Fig. 61. 2070.



Record from which the measurements were taken for the construction of the curves in preceding figure. Excitation in pairs, first with descending break, then with ascending break, only the former being used for the curves.

§ 5. *Theoretical Considerations.*

In conclusion, but explicitly recognizing that the conclusion may be otherwise stated in the particular terminology of electrotonic phenomena, we may admit as a general theory, embracing the positive and negative expressions of action in living nerve, excited by electrical stimulation, that :

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* Corrected as described on p. 66, note to Table D.

Neuroplasm[*] *is chemically mobile in two directions, downwards in the direction of disintegration, upwards in the direction of integration.*

Although we are often constrained to refer to these two opposite aspects of metabolism as two opposite processes—a negative process, disintegration, dissimilation, analysis, katabolism as opposed to a positive process, integration, assimilation, synthesis, anabolism—they should not be imagined as distinct, but as conjoined in one actually indivisible complex change. We may not suppose that we ever witness the simple effect of a positive or of a negative process acting alone, but always the resultant effect of a process in which negative predominates over positive, or *vice versâ*. The process behind its negative or its positive manifestation is not exclusively negative or exclusively positive, but negative (and positive), or positive (and negative).[†]

In terms of this hypothesis or figment, the phenomena previously described relating to the three states of nerve, may be expressed as follows:—

1. In fresh nerve ("first state"), containing neuroplasm highly wound up, *i.e.*, capable of unwinding, excitation, which augments the negative-cum-positive process, elicits a manifest negative resultant, signified galvanometrically by a negative deflection. During the period subsequent to predominant disintegration, reintegration is predominant, but since the conjoint positive-cum-negative process is taking place in neuroplasm that is still at a high level, that positive predominance is slight and the positive after-effect is small.

2. In stale nerve ("third state"), containing neuroplasm that has run down, *i.e.*, that is capable of being wound up, excitation, which augments the negative-cum-positive process, elicits a manifest positive resultant, and there is, *even during excitation*, a predominant integration, signified galvanometrically by a positive deflection.

This predominance of positive over negative diminishes during tetanisation (? by reason of CO_2), and may give way to a predominance of negative over positive. So long as there is positive predominance during excitation, the deflection (ω), at its close, will be negative (fig. 45); when negative predominance has set in during excitation, the deflection (ω), at its close, will be positive (fig. 46). (In the former case, the "disguised" effect of CO_2 is witnessed, in the latter, the "clear" effect.)

3. In "transitional" nerve ("second state") containing neuroplasm that is half run down, capable therefore of being wound up or unwound, the negative factor predominates during excitation, and the positive factor predominates after excitation.

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[*] Using the term "neuroplasm" to denote the living excitable matter that forms the axis-cylinder of a medullated fibre, in distinction from the sheath itself which, in relation to the medulla, is the "trophoplasm."

[†] The ordinary "negative variation" of nerve, due to predominant negative change at and near the longitudinal lead-off, is itself probably (if not demonstrably) composed of two factors—negative predominant over positive near the longitudinal lead-off, and positive predominant over negative near the transverse lead-off.

The disposition to movement in one or other direction is more nearly equipoised than in either the first or the third states.

4. In all states of nerve the negative change is promoted by little CO_2, obstructed by much CO_2.

5. In all states of nerve the usual effect of prolonged tetanisation is an augmentation of the negative mobility (augmented S in the 1st and 2nd states, figs. 29, 35; diminished N and reversal from N to S in the 3rd state, figs. 30, 32); the exceptional effect of tetanisation is a diminution of the negative mobility (diminished S in the 2nd state, fig. 37; increased N in the 3rd state, fig. 36).

Expressed in terms of electrotonic changes K and A, the same series of facts may be clothed in the following statements, involving less assumption, but also offering less explanation:—

1. In fresh nerve (1st state) the sum of propagated katelectrotonic effects exceeds the sum of propagated anelectrotonic effects—$K > A$. Therefore, negative deflection during tetanisation.

2. With lapse of time, the difference $K > A$ diminishes to $K = A$, and becomes reversed to $K < A$. Therefore, positive deflection during tetanisation.

3. The effect of CO_2 in small quantity is to augment K. Therefore, augmented negative deflection of the 1st and 2nd states; diminution or reversal of the positive deflection of the 3rd state.

4. The effect of CO_2 in large quantity is to diminish K. Therefore, diminution or abolition of negative deflection of 1st and 2nd states.

5. The usual effect of tetanisation is augmented K; the exceptional effect of tetanization is diminished K.

6. During prolonged tetanisation the difference $K > A$ of the 1st and 2nd states gradually increases, and the difference $A > K$ of the 3rd state gradually diminishes. Therefore, the deflection during such tetanization is increasingly negative or diminishingly positive.

7. If during prolonged tetanisation of nerve in the 3rd state, the diminishing difference $A > K$ reaches to reversal, viz., to $K > A$, the deflection at the end of tetanisation is positive; fig. 46. If the difference $A > K$ does not reach to equality, $A = K$, the deflection at the end of tetanisation is negative; fig. 45.

§ 6. *Concerning the Unfatiguability of Nerve.*

The experimental inexhaustibility of nerve-fibres as compared with the rapid exhaustibility of nerve-terminals, upon which, in common with WEDENSKI and BOWDITCH, I have formerly laid much stress, and which, as mentioned in Chapter I. (p. 2), formed one of the starting-points of this investigation, presents itself with a very different and far more readily intelligible significance by the light of these considerations, fortified by what I am tempted to designate as proof of a chemical alteration in tetanised nerve. And in this connection it is of little moment whether we hold, with **Hering**, that negative effects and positive after-effects are the signs of dissimilation and assimilation, or with **Hermann**, that they are of electrotonic nature --the signs of the extraordinarily rapid polarisation and depolarisation characteristic of living medullated nerve.* Medullated nerve-fibres are experimentally inexhaustible, not because their tetanisation effects little or no chemical change, but because such change is extremely rapid and rapidly effaced by a change in an opposite direction. The materials of which normal medullated nerve is composed (grey "neuroplasm" and white "trophoplasm") are in a state of great chemical lability, so that whatever is done, is done easily, and as easily undone.† That something is done (or rather undone) during nerve-tetanisation, has, I think, been proved by the series of experiments described in Chapter III.; and towards the determination of what that something may be, I have also brought evidence, if not proof, that one at least of its terminal products is carbon dioxide.

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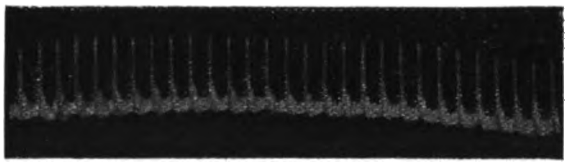
* **Hermann.** 'Polarisation der Muskeln und Nerven.' **Pflüger's** 'Archiv,' vol. 42, 1888.

† At the last Physiological Congress (Berne, 1895) records were exhibited of the retinal currents of action provoked by illumination at regular intervals, and demonstrating that the retina resembles nerve with respect to its inexhaustibility. The interpretation given above for nerve—viz., apparent inexhaustibility as being in reality rapid disintegration effaced by rapid reintegration—applies with even greater probability to retinal phenomena, where, chiefly by reason of **Hering's** arguments, we have already been familiarized with the dual aspect of metabolism. The fact that the retina exhibits no sign of fatigue is indeed, in some degree, a collateral item of evidence in the direction of the conclusion *re* nerve. It may scarcely be doubted that the retina excited by light suffers chemical change, and it may be demonstrated that the retina submitted to a practically interminable series of flashes exhibits no signs of expenditure of matter, the strict conclusion is, therefore, that disintegration is effaced by reintegration.

Fig. 62. (Plate 51.)



February 5, 1895.—Portion of a prolonged series of retinal deflections caused by stimulation of the frog's eyeball at intervals of one minute. Each stimulation consists in the light of a standard candle at a distance of two feet acting for a period af $7\frac{1}{2}$ seconds. The electromotive value of each deflection is about 0·0001 volt.

TABLE D.—Measurements of some of the Observations given in Tables B and C.

NOTE.—In most experiments a partially damped Thomson galvanometer (R = 15,000 ohms.) was used, shunted if necessary. In some of the experiments the position of the controlling magnet was such that the suspended system of magnets oscillated between 4 and 5 times per minute (period = 12 to 15 secs., decrement = 2·8 to 3). In others the oscillation frequency was 7 per minute (period = 8·5 secs., decrement = 2).

In any evaluation of after-deflection this purely instrumental oscillation must be reckoned with, and to this end it is best to take the relation between swing and swing-back by letting a small E.M.F. into the circuit for 7½ seconds (*i.e.*, through the mercury pool to be used in the exciting circuit). The corresponding correction of after-deflection is made throughout the numbers given in Table D.

In later experiments I employed a less sensitive, but perfectly dead-beat galvanometer (by Messrs. MUIRHEAD & Co.), the rising or falling time of which was 12 seconds. With the partially damped galvanometer any positive or negative after-effect obtaining during the first few (2 to 7) seconds after the end of excitation was manifested as an augmentation or diminution of the instrumental swing-back; with the aperiodic instrument any such after-effects occurring during the falling time (12 seconds) were lost to view, and only such as remained present after the expiration of that time were manifested. Plate 2175 exhibits the photogram of the dead-beat instrument acted upon by $\frac{1}{1000}$ volt for 1 minute. Plate 2177 is an example of a normal tracing of nerve in a late first or early second stage, the duration of tetanus at 10 units being 15 seconds. It exhibits the gradual decline of a positive after-effect, such as was observed by HERING, and which in my view is a gradually increasing effect of CO_2. Plates 2181, 2185, 2195, 2200, 2203, 2204, 2207, 2208 were likewise recorded with the dead-beat gavanometer. All others were taken with the same partially damped instrument.

The capillary electrometer is in many respects the best instrument of all for obtaining a dead-beat record of the entire effect and after-effect of tetanisation. For various reasons that need not be detailed, I have not yet employed this instrument systematically, but only occasionally, and shall, therefore, not further consider it at this juncture.

The numbers indicate millimeters of deflection (Column I.) and of after-deflection (Column II.). The latter series of numbers requires to be corrected for oscillation, as stated in text. To this end, in observations after No. 675, a key-plate is taken by sending a small E.M.F. into circuit once a minute through the mercury pool (7·5 seconds), to be used in the exciting circuit.

Plate 763 (7 oscillations per minute) is the key-plate to Nos. 675, 676, 678, 680, 689, 710, 711, 737 741, 745, 747, 751, 752, 761, 762, 782.

Plate 2041 (between 4 and 5 oscillations per minute, more rapidly moving surface) is the key-plate to Nos. 825, 843, 857, 858, 859, 869, 874, 898, 905, 912, 928, 929, 933, 935, 937, 942, 958, 960, 982, 983, 984, 985, 990, 991, 993, 994, 2003, 2004, 2005, 2006, 2054, 2055, 2057, 2068, 2069, 2072, 2073, 2074, 2075, 2080, 2081, 2082, 2084.

Correction is accordingly made by subtracting from the after-deflection (Column II.) either one-third or two-thirds of the corresponding deflection in Column I., thus yielding a net value in estimation of after-effect due to the nerve.

Great accuracy may not be claimed for such an estimate; the key-plate 763 shows considerable irregularity of swing-back, which, however, was much diminished in subsequent experiments. The net values, after subtraction of one-third deflection, can, therefore, only be approximately correct, and none but well-marked alterations of such values may be admitted to rank as assured data. Key-plate 2041 is more regular, but in the group of experiments to which it belongs the controlling magnet was slipped slightly up and down during adjustment; the oscillation frequency was thus varied between a little more and a little less than 4·5 oscillations per minute, and a relation between swing-back and swing that was ·6 at the higher and ·66 at the lower frequency.

These considerations apply only to the after-deflection, not to the deflection, and are entered upon to show within what range of error the former may be estimated. Looking back to records taken when no heed was paid to the after-effect, it is still possible to form some judgment as to its presence and amount. Instances of such retrospective estimates are given at the end of Table D, referring to some of the plates figured in the paper, viz., Nos. 200, 309, 334, 537, 708; the two pairs of records here figured, 3180–1, 3188–9, with their measurements, are given to show how the oscillating and dead-beat instruments respond to the same electromotive change, and to what extent the corrected measurements of the oscillating instrument are to be trusted.

With the oscillating magnet (5 osc. per minute) the net after-deflection is due to the state of nerve during the 2 to 3 seconds succeeding the end of excitation; with the fully damped magnet (falling time = 12 seconds), any after-deflection is due to the state of nerve during the period commencing 12 seconds after the end of excitation. So that the indications of the two instruments are complementary, the first being that of the beginning and the second that of the tail of the after-effect in the nerve. The two indications have always been of the same sign, the former being the more sensitive of the two. It was frequently noticed that the same nerve giving a considerable net after-deflection to the oscillating magnet, manifested no sensible after-deflection to the damped instrument.

Fig. 63. Key-plate 763.

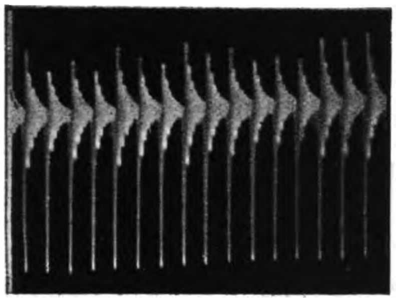


Fig 64. Key-plate 2041.

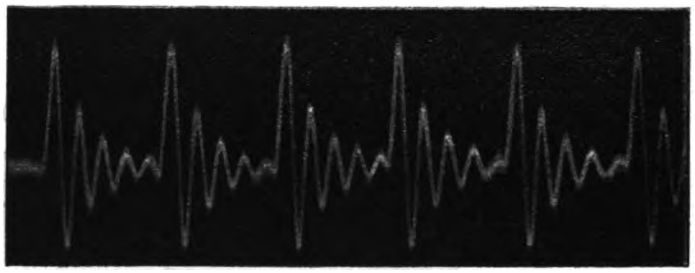


Fig. 65.

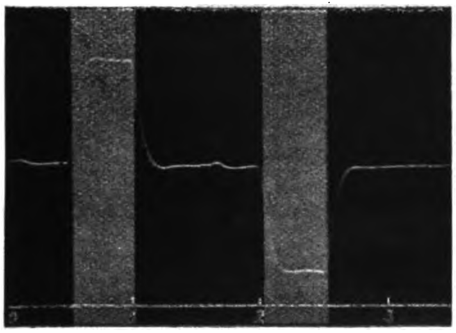


Fig. 66. (Obs. 2177.)

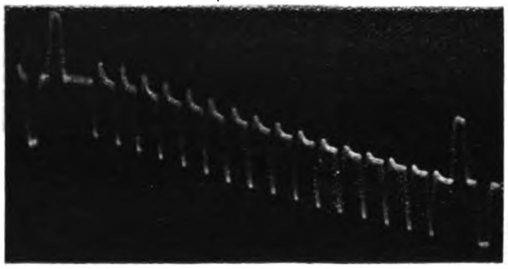
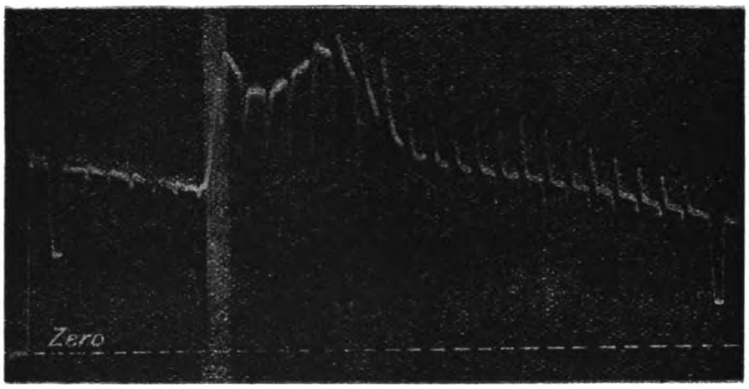


Fig. 65.—Record by the dead-beat galvanometer of an E.M.F. of 0·001 volt through a nerve, first in one, then in the opposite direction; time of closure = $\frac{1}{2}$ minute.

To show the falling time (= 10 to 12 seconds), and that the galvanometer is sufficiently dead-beat to permit us to take an excursion above the line, as in Plate 2177, to be significant of positive after-effect.

Fig. 66.—February 10, 1896.—Nerve in the late first or early second stage. To show the progressive diminution of the positive after-deflection.

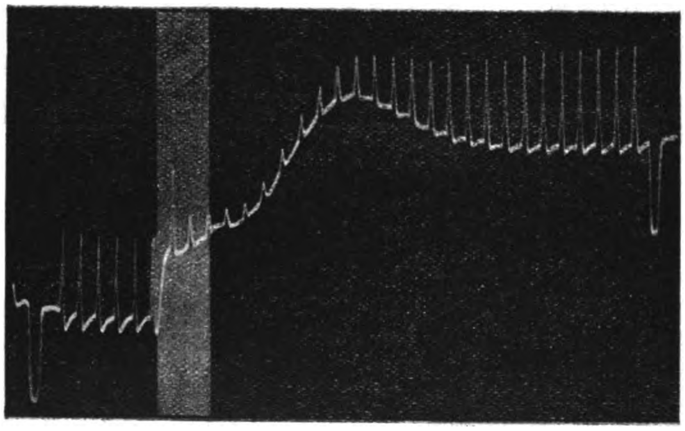
Fig. 67. (Obs. 2249.)



Record by dead-beat galvanometer of the effect of carbon dioxide on a very small negative variation (Connections as in fig. 3.)

This figure exhibits a point that has not been commented upon in the text, but is frequently witnessed in prolonged experiments, viz., a greatly augmented positive after-effect subsequent to the primary or secondary increase of the negative effect.

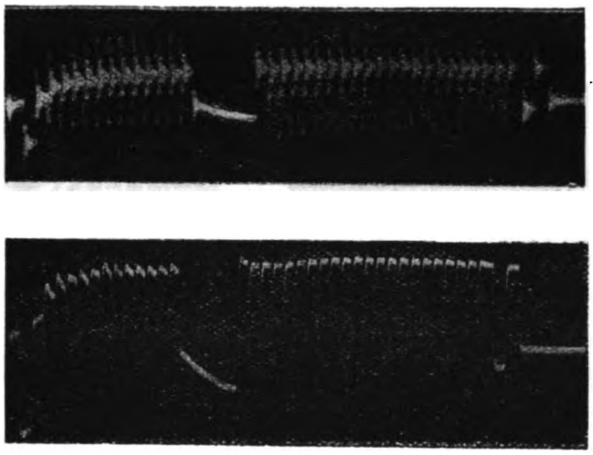
Fig. 68. (Obs. 2169.)



Record by dead-beat galvanometer of the effect of ether upon auelectrotonus. (Connections as in fig. 48, D.)

(NOTE.—Figs. 63–70 were added July 30, 1896.)

Fig. 69.

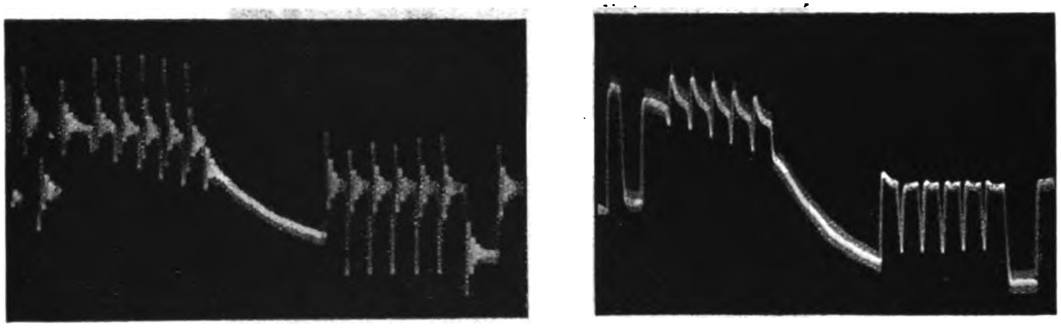


Simultaneous record of an experiment on the partially damped and fully damped galvanometers in circuit. The former, 3180, T., is shunted to ¼, oscillates 5 times per minute, and with the closure time of 7·5 seconds gives a swing-back = ⅔rds the original swing. The latter, 3181, M., is not shunted, and has a falling-time of 12 seconds.

The two records, which exhibit the ordinary result of prolonged tetanisation, are given in explanation of the correction to be made for oscillation (3180, T.). In 3181, M., the closure-time being shorter than the falling-time, the negative variations do not reach their maximum. In 3180, T., the net after-effect is due to the state of nerve during the 2 to 3 seconds immediately after the 7½ seconds excitation; in 3181, M., any positive after-effect would be due to the state of nerve during the last ⅔rds of each minute. Such positive after-effect is better seen in plate 2177 (fig. 3B).

	Time.	I.	II.	(·6 I.)	II. net.	I./II.	0·001 volt.
	minutes.						
3180, T.	1	− 3·5	+5·7	(2·1)	+3·6	..	9·5
	2	− 5·3	+5·7	(3·2)	+2·5		
	3	− 6·0	+5·7	(3·6)	+2·1		
	5	− 6·0	+5·5	(3·6)	+1·9		
	12	− 6·5	+5·0	(3·9)	+1·1		
		Tetanisation, 10 units, 5 minutes					
		α = − 6·5		ω = + 11·5			
	19	− 9·5	+5·5	(5·7)	−0·2		
	25	− 8·5	+5·0	(5·1)	−0·1		
	30	− 8·5	+5·0	(5·1)	−0·1		
	32	− 8·0	+5·0	(4·8)	−0·2	..	8·7
3181, M.	1	− 4	+4	..	..	..	13·5
	2	− 6	+2·5				
	3	− 6·5	+1·5				
	5	− 7	+1·2				
	12	− 7·5	+1				
		Tetanisation, 10 units, 5 minutes					
		α = − 10·5		ω = + 17			
	19	−11	0				
	25	−10	0				
	30	− 9·5	0				
	39	− 9	0	..	..	..	13·5

Fig. 70.



3188, T. 3189, M.

Simultaneous record of an experiment (influence of tetanisation on nerve in the second stage) on the partially damped and fully damped galvanometers in circuit.

	Time.	I.	II.	(·57 I.)	II. net.	I./II.	0·001 volt.
	minutes.						
3188, T.	0	− 3·2	+8·0	(1·8)	+6·2	..	15
	1	− 4·8	+9·4	(2·7)	+6·7		
	2	− 5·4	+9·6	(3·1)	+6·5		
	3	− 6·2	+9·5	(3·5)	+6·0		
	4	− 6·4	+9·4	(3·6)	+5·8		
		Tetanisation, 10 units, 5 minutes $\alpha = -6·5$ $\omega = +13·5$					
	11	−12	+4·0	(6·8)	−2·8		
	12	−12	+5·5	(6·8)	−1·3		
	13	−11·5	+5·3	(6·6)	−1·3		
	14	−11·5	+6·0	(6·6)	−0·6		
	15	−11·5	+6·5	(6·6)	−0·1	..	14·5
3189, M.	0	− 2	+4	..	..	..	14
	1	− 3·3	+3·5				
	2	− 3·8	+3·2				
	3	− 4·2	+2·8				
	4	− 4·5	+2·5				
		Tetanisation, 10 units, 5 minutes $\alpha = -4·8$ $\omega = +11·5$					
	11	− 9·3	0				
	12	− 9	0				
	13	− 9	0				
	14	− 8·8	0				
	15	− 8·5	0	..	..	..	13

TABLE D (continued).—Measurements of some of the Observations given in Tables B and C.

	Time. minutes.	I.	II.	($\frac{1}{3}$ I.)	II. net.	I./II.	0·001 volt.
675 (fig. 29)	0	−13	+ 7·5	(4·3)	+ 3·2	4·1	26
		Tetanisation, 10 units, 5 minutes $\alpha = -13$ $\omega = +28$					
	6	−20	+12·5	(6·7)	+ 5·8	3·45	
	11	−16	+11	(5·3)	+ 5·7	2·8	
	16	−12	+ 7·5	(4)	+ 3·5	3·4	
	21	−10	+ 6·5	(3·3)	+ 3·2	3	24
676	0	−10	+10	(3·3)	+ 6·7	1·5	8
		Tetanisation, 10 units, 10 minutes $\alpha = -10$ $\omega = +19$					
	11	−14·5	+12·5	(4·8)	+ 9·7	1·5	
678	0	−10	+20	(3·3)	+16·7	0·60	18
		Tetanisation, 10 units, 10 minutes $\alpha = -10$ $\omega = +31·5$					
	11	−16	+21·5	(5·3)	+16·2	0·99	
	21	−13	+21·5	(4·3)	+17·2	0·76	
	31	−11	+16·5	(3·7)	+12·8	0·86	
	41	− 9	+14·5	(3)	+11·5	0·77	17
680	0	− 8·5	+18	(2·7)	+15·3	0·55	21
		Tetanisation, 10 units, 10 minutes $\alpha = -9$ $\omega = +29$					
	11	−16	+21	(5·3)	+15·7	1·02	
	21	−14	+20·5	(4·7)	+15·8	0·88	
	31	−10	+18	(3·3)	+14·7	0·68	
	40	− 9	+15·5	(3)	+12·5	0·72	18
689	0	−10	+14	(3·3)	+11·7	0·85	22
		Tetanisation, 10 units, 20 minutes $\alpha = -9$ $\omega = +27$					
	21	−18	+17·5	(6)	+11·5	1·57	
	26	−16	+14·5	(5·3)	+ 9·2	1·74	
	31	−15	+14	(5)	+ 9	1·67	
	36	−14	+14	(4·7)	+ 9·3	1·51	19

TABLE D (continued).—Measurements of some of the Observations given in Tables B and C.

	Time.	I.	II.	($\frac{1}{3}$ I.)	II. net.	I./II.	0·001 volt.
	minutes.						
710 (fig. 35)	0	− 7	+19	(2·3)	+16·7	0·42	13
		CO_2 for 1 minute					
	2	−14	+ 6	(4·7)	+ 1·3	10·7	
	7	−12	+ 4	(4)	+ 0		
	12	−22	+28	(7·3)	+20·7	1·05	11·5
711	0	− 2·5	+18·5	(0·8)	+17·7	0·14	11
	4	− 3·5	+17·5	(1·2)	+16·3	0·21	
CO_2	5	−15	+ 7	(5)	+ 2	7·5	
	7	− 7·5	+ 2·5	(2·5)	+ 0		
	9	− 8	+ 2	(2·7)	− 0·7		
	11	− 8·5	+ 3	(2·8)	+ 0·2		
	14	− 9	+ 3	(3)	0		
	15	− 9·5	+ 4	(3·2)	+ 0·8	12	
	17	−16	+ 7·5	(5·3)	+ 2·2	7·3	
	20	−32	+17·5	(10·7)	+ 6·8	4·7	
	23	−27·5	+27·3	(9·2)	+18·1	1·3	10
737	0	− 2	+ 6	(0·7)	+ 5·3	0·38	
		Tetanisation, 10 units, 5 minutes					
	6	− 7	+ 9·5	(2·3)	+ 7·2	0·98	
	7	− 7	+12	(2·3)	+ 9·7	0·72	
	8	− 8	+13·5	(2·7)	+10·8	0·74	
741	0	−24	+17·5	(8)	+ 9·5	2·5	12
		Tetanisation, 10 units, 5 minutes $\alpha = -25$ $\omega = +39$					
	6	−29	+20·5	(9·7)	+10·8	3·7	
	11	−28	+20	(9·3)	+10·7	3·8	
	16	−27	+19	(9)	+10	2·7	
745	1	− 4	+ 5	(1·3)	+ 3·7	..	27
	4	− 4	+ 5	(1·3)	+ 3·7		
CO_2	5	−14	+ 2	(4·7)	− 2·7		
	6	− 3·5	0	(1·2)	− 1·2		
	7	− 2	0	(0·7)	− 0·7		
	8	− 3·5	0	(1·2)	− 1·2		
	9	− 7·5	0	(2·5)	− 2·5		
	10	−15	0	(5)	− 5		
	11	−22·5	+ 7	(7·5)	− 0·5		
	12	−27·5	+ 8	(9·2)	− 1·2		
	13	−28	+11	(9·3)	+ 1·7		
	14	−25·5	+15	(8·5)	+ 6·5		
	15	−23	+17	(7·7)	+ 9·3		
	16	−20	+19	(6·7)	+12·3		
	17	−19	+21	(6·3)	+14·7		

Table D (continued).—Measurements of some of the Observations given in Tables B and C.

	Time.	I.	II.	(⅓ I.)	II. net.	I./II.	0·001 volt.
	minutes.						
747	0	− 4·5	+ 4·5	(1·5)	+ 3	..	15
	5	− 3·5	+ 4	(1·2)	+ 2·8		
	10	− 3	+ 3·5	(1)	+ 2·5		
CO$_2$	11	− 2	+ 2	(0·7)	+ 1·3		
	12	− 2	+ 2	(0·7)	+ 1·3		
	13	− 5	+ 7	(1·7)	+ 5·3		
	14	−12	+ 7	(4)	+ 3		
	19	−17·5	+11	(5·8)	+ 5·2		
	20	−17·5	+10	(5·8)	+ 4·2		
CO$_2$	21	−12	0	(4)	− 4		
	22	− 9	0	(3)	− 3		
	23	− 7·5	0	(2·5)	− 2·5		
	24	− 8	0	(2·7)	− 2·7		
	25	−10	0	(3·3)	− 3·3		
	30	−24	+ 9	(8)	+ 1		
	35	−14	+ 9	(4·7)	+ 4·3		
	40	− 7	+ 6	(2·3)	+ 3·7	..	14
751	0	+ 2	+ 9	(0·67)	+ 9·67		
		Tetanisation, 10 units, 5 minutes $\alpha = +2$ $\omega = +9$					
	6	− 5	+ 9·5	(1·67)	+ 7·83		
	11	− 4·5	+ 9	(1·5)	+ 7·5		
	16	− 4	+ 8	(1·33)	+ 6·7		
	21	− 3·5	+ 8	(1·2)	+ 6·8		
752	0	− 3	+ 8	(1)	+ 7		
	7	− 3	+ 8	(1)	+ 7		
		CO$_2$ for 1 minute					
	10	− 0·5	0	(0·2)	− 0·2		
	11	− 1	0	(0·3)	− 0·3		
	12	− 3·5	0	(1·2)	− 1·2		
	13	− 8·5	+ 3·5	(2·8)	+ 0·7		
	14	−15	+ 7·5	(5)	+ 2·5		
	15	−15	+ 8·5	(5)	+ 3·5		
	20	− 7·5	+12	(2·5)	+ 9·5		
	25	− 6·5	+ 8	(2·2)	+ 5·8		
	30	− 5	+ 7·5	(1·8)	+ 5·7		
761	0	− 7	+ 4	(2·3)	+ 1·7	4·1	26
		Tetanisation, 10 units, 5 minutes $\alpha = -7$ $\omega = +14$					
	6	−11	+ 6	(3·7)	+ 2·3	4·8	
	11	−10	+ 5	(3·3)	+ 1·7	5·9	
	16	− 9	+ 4	(3)	+ 1	9·0	26

Table D (continued).—Measurements of some of the Observations given in Tables B and C.

	Time.	I.	II.	(⅓ I.)	II. net.	I./II.	0·001 volt.
	minutes.						
762	0	− 4·5	+ 11·5	(1·5)	+ 10	0·45	22
		Tetanisation, 10 units, 5 minutes α = − 4·5 ω = + 24					
	6	−12	+13·5	(4)	+ 9·5	1·26	
	11	−10	+12	(3·3)	+ 8·7	1·13	
	16	− 9	+11·5	(3)	+ 8·5	1·06	
782	0	+11	− 1·5	(3·7)	+ 1·2		25
	4	+11	− 1·5	(3·7)	+ 1·2		
		Tetanisation, 10 units, 5 minutes α = + 11 ω = − 11					
	10	+11	− 3·5	(3·7)	+ 0·2		
	15	+11·5	− 1·0	(3·8)	+ 2·8		
	20	+12·5	− 1·0	(4·2)	+ 3·2		23

	Time.	I.	II.	(⅓ I.)	II. net.	I./II.	0·001 volt.
	minutes.						
857	0	− 2	+ 8	(1·3)	+ 6·7	3·3	15·5
		Tetanisation, 5 minutes, 10 units α − 2 ω + 21·5					
	6	−12·5	+10	(8·5)	+ 1·5	8·3	
	11	− 8	+ 9·5	(5·4)	+ 2·6	3·1	
	16	− 5·5	+ 8·5	(3·7)	+ 1·8	3	
858 (fig. 30)	0	+ 7	+ 1	(4·7)	+ 5·7	..	13·5
		Tetanisation, 5 minutes, 10 units α + 5 ω + 17					
	6	− 9	+ 8	(6)	+ 2	4·7	
	11	− 4·5	+ 7	(3)	+ 4	1·1	
	16	− 1·5	+ 5	(1)	+ 4	·37	
859 (fig. 31)	0	+ 8	− 1	(5·4)	+ 4·4		
		CO_2, 3 minutes					
	10	− 9	+10	(6)	+ 4	2·3	
	15	− 2·5	+ 8·5	(1·7)	+ 6·8	0·3	

Table D (continued).—Measurements of some of the Observations given in Tables B and C.

	Time.	I.	II.	(⅔ I.)	II. net.	I./II.	0·001 volt.
	minutes.						
869	0	−7	+4·5	(4·7)	−0·2		
(fig. 16)	5	−7	+4·5	(4·7)	−0·2		
CO$_2$	6	−7	(?)				
	7	−13	+8·5	(8·7)	−0·2		
	8	−14·5	+6·5	(9·7)	−3·2		
	9	−14·5	+7·0	(9·7)	−2·7		
	10	−15·5	+8·0	(10·3)	−2·3		
	11	−16	+9·0	(10·7)	−1·7		
	12	−17	+10·0	(11·3)	−1·3		
	13	−17·5	+10·5	(11·7)	−1·2		
	14	−18	+12·0	(12)	0		
	15	−17·5	+12·0	11·7	+0·3		
	20	−15	+11·5	10	+1·5		
	25	−12	+9·5	8	+1·5		
874	0	+15	−11	(10)	−1	..	11
	5	+15	−10	(10)	0		
		Tetanisation, 10 units, 5 minutes					
		α = + 15		ω = − 7			
	11	+12	−5	(8)	+3		
	16	+11	−5	(7·3)	+2·3		
	21	+11·5	−6	(7·7)	+1·7		
	26	+12	−6·5	(8)	+1·5		
905	0	+12	−7	(8)	+1	..	16
(fig. 36)	8	+11	−7	(7·3)	+0·3		
		Tetanisation, 10 units, 10 minutes					
		α = + 11·5		ω = − 15·5			
	20	+14	−9·5	(9·3)	−0·2		
	30	+13	−8	(8·7)	−0·7		
	40	+13	−8	(8·7)	−0·7		
	50	+12	−7·5	(8)	+0·5	..	14
912	0	−7	+13	(4·7)	+8·3	..	14
(fig. 37)	11	−7·5	+13	(5)	+8		
		Tetanisation, 10 units, 10 minutes					
		α = − 9		ω = + 11			
	22	−5	0	(3·3)	+3·3		
	30	−8	+6·5	(5·3)	+1·2		
	40	−10·5	+9·5	(7)	+2·5		
	50	−10	+9·5	6·7	+2·8	..	12·5

TABLE D (continued).—Measurements of some of the Observations given in Tables B and C.

	Time.	I.	II.	($\frac{2}{3}$ I.)	II. net.	I./II.	0·001 volt.
	minutes.						
928	0	− 8·5	+ 9·5	(5·65)	+3·85	2·2	19·5
		Tetanisation, 5 minutes, 10 units α − 8 ω + 43					
	6	−31	+26	(20·7)	+5·3	5·85	
	11	−21	+19	(14)	+5	4·2	
	16	−14·5	+14·5	(9·35)	+5·15	2·8	
	21	−10	+10	(6·7)	+3·3	3	
929	0	− 1	+ 3·5	(·67)	+2·83	1·23	18
		Tetanisation, 5 minutes, 10 units α − 1 ω + 26·5					
	6	−18·5	+15	(12·3)	+2·7	6·9	
	11	− 9	+ 8·5	(6)	+2·5	3·6	
	16	− 4	+ 5·5	(2·7)	+2·8	1·4	
	21	− 1·5	+ 1·5	(1)	+ ·5	3	
933 (fig. 40)	0	+ 7	−10	(4·7)	−5·3	..	17·5
		Tetanisation, 5 minutes, 10 units α + 6·5 ω + 30					
	6	−15·5	+16	(10·3)	+5·7		
	11	− 5·5	+ 5	(3·7)	+1·3		
	16	+ 1·5	− 7	(1)	−6		
	21	+ 4·5	− 9	(3)	−6		
935	0	− 7	+ 8	4·7	+3·3	..	5·5
	5	− 6·5	+ 7·5	4·3	+3·2		
CO_2	6	− 5·5	+ 8	3·7	+4·3		
	7	− 8·5	+ 7·5	5	+2·5		
	8	−11·5	+ 4·5	7·7	−3·2		
	9	−10·5	+ 2·5	7	−4·5		
	10	− 8·5	+ 1·5	5·7	−4·5		
	11	− 6·5	+ 1	4·3	−3·3		
	12	− 7	+ 1·5	4·7	−3·2		
	13	− 9	+ 3·5	6	−2·5		
	14	−13·5	+ 6·5	9	−2·5		
	15	−17	+ 9·5	11·3	−1·8		
	20	−11	+11	7·3	+3·7		
	25	− 8·5	+10·5	5·7	+4·8		
937	0	− 6	+ 6	(4)	+ 2	3	10·5
		Tetanisation, 10 units, 5 minutes $\alpha = -7$ $\omega = +21$					
	6	−11	+ 8	(7·3)	+0·7	15·7	
	11	− 8·5	+ 7	(5·7)	+1·3	6·5	
	16	− 8	+ 6·5	(5·3)	+1·2	5·4	
	21	− 7	+ 6·5	(4·7)	+1·8	3·6	

Table D (continued).—Measurements of some of the Observations given in Tables B and C.

	Time.	I.	II.	(⅔ I.)	II. net.	I./II.	0·001 volt.
	minutes.						
942	0	+11	− 8	(7·3)	− 0·7	11·4	35
		Tetanisation, 10 units, 5 minutes $\alpha = +11$ $\omega = -23·5$					
	6	+13·5	−16	(9)	− 7	1·74	
	11	+11·5	−10·5	(7·7)	− 2·8	4·1	
	16	+11·5	− 9·5	(7·7)	− 1·8	6	
958	0	− 3	+13·5	(2)	+11·5	0·26	23·5
	1	− 6·5	+15	(4·3)	+10·7	0·61	
	2	− 8·5	+15	(5·7)	+ 9·3	0·91	
	3	− 9·5	+15	(6·3)	+ 8·7	1·09	
	4	−10	+15	(6·7)	+ 8·3	1·20	
	5	−11	+15	(7·3)	+ 7·7	1·41	
	6	−11·5	+15	(7·7)	+ 7·3	1·58	
	7	−11·5	+15	(7·7)	+ 7·3	1·58	
	8	−11·5	+15	(7·7)	+ 7·3	1·58	
		Tetanisation, 10 units, 5 minutes $\alpha = -12$ $\omega = +36$					
	14	−26	+16·5	(17)	− 0·5		
	19	−22	+16	(15)	+ 1·0	22	
		Pause of 5 minutes					
	25	−13	+14	(8·6)	+ 5·4	2·4	
	30	−15	+15	(10)	+ 5	3	
960 (fig. 42)	1	+ 5	+15	(3·3)	+18·3	..	38
	5	0	+14	0			
		Tetanisation, 10 units, 5 minutes $\alpha = 0$ $\omega = +45·5$					
	12	−34	+19·5	22·7	− 3·2		
	15	−30	+17·5	20	− 2·5		
	20	−25	+17	16·7	+ 0·3		
	25	−21·5	+17	14·3	+ 2·7	..	38
982 (fig. 26)	0	+14	− 8·5	(9·3)	+ 0·8	..	19·5
	5	+11·5	− 8	(7·7)	− 0·3		
		CO_2 for 1 minute					
	6	+12	− 7	(8)	+ 1·0		
	7	+ 8	− 4	(5·3)	+ 1·3		
	8	+ 7	− 2·5	(4·7)	+ 2·2		
	10	+ 5	− 1·5	(3·3)	+ 1·8		
	14	+ 7	− 2	(4·7)	+ 2·7		
	20	+ 9	− 3·5	(6·0)	+ 2·5		
	25	+ 9·5	− 4·5	(6·3)	+ 1·8		
	29	+10	− 5·5	(6·7)	+ 1·2		

Table D (continued).—Measurements of some of the Observations given in Tables B and C.

	Time.	I.	II.	(⅔ I.)	II. net.	I./II.	0·001 volt.
	minutes.						
983	0	+11·5	− 7	(7·7)	+ 0·7	..	19·5
	5	+11·5	− 7	(7·7)	+ 0·7		
CO_2	6	0	0				
	7	0	0				
	8	− 2	0	(1·3)	+ 1·3		
	9	− 2	0	(1·3)	+ 1·3		
	12	+ 3·5	− 5	(2·3)	− 2·7		
	13	− 3	?				
	14	− 4	+ 3	(2·7)	+ 0·3		
	15	− 5	+ 4	(3·3)	+ 0·7		
	16	− 5·5	+ 5·5	(3·7)	+ 1·8		
	17	− 7	+ 7	(4·7)	+ 2·3		
	18	− 5·5	+ 7·5	(3·7)	+ 3·8		
	19	− 3·5	+ 7	(2·3)	+ 4·7		
	20	0	+ 6	(0)	+ 6·0		
	21	+ 2	+ 5	(1·3)	+ 6·3		
	22	+ 3·5	+ 4·5	(2·3)	+ 6·8		
	23	+ 5·5	+ 4·5	(3·7)	+ 8·2		
	24	+ 6·5	+ 4·5	(4·3)	+ 8·8		
	25	+ 7·5	+ 5	(5)	+10		
984 (fig. 32)	0	+14·5	− 6·5	(9·7)	+ 3·2	..	19
	5	+13·5	− 7	(9)	+ 2		
		Tetanisation, 10 units, 5 minutes					
		α = + 13·5		ω = − 2·5			
	11	+ 5·5	− 2·5	(3·7)	+ 1·2		
	16	+ 9·5	− 4·5	(6·3)	+ 1·8		
	21	+10·5	− 6·5	(7)	+ 0·5		
	25	+12	− 7·5	(8)	+ 0·5		
985	0	+14·5	− 8·5	(9·7)	+ 1·2	..	19
	5	+14·5	− 8·5	(9·7)	+ 1·2		
		Tetanisation, 10 units, 5 minutes					
		α = + 14·5		ω = − 6·5			
	11	+ 8·5	− 6	(5·7)	− 0·3		
	16	+10·5	− 7	(7)	0		
	21	+12	− 8	(8)	0		
990	0	+21	−13	(14)	+ 1	..	54
			CO_2 for 1 minute				
	1	+20	−10	(13·3)	+ 3·3		
	5	+ 1·5	+ 5	(1)	+ 4		
	10	+ 5·5	+ 5·5	(3·7)	+ 1·8		
	15	+12	− 4	(8)	+ 4		
	20	+14	− 6	(9·3)	+ 3·3		

Table D (continued).—Measurements of some of the Observations given in Tables B and C.

	Time.	I.	II.	(⅔ I.)	II. net.	I./II.	0·001 volt.
	minutes.						
991	0	− 4·5	+ 9	(3)	+ 6	..	23
		Tetanisation, 10 units, 5 minutes					
		$\alpha = -4{\cdot}5$			$\omega = +12$		
	6	− 5·5	+ 9·5	(3·7)	+ 5·8		
	11	− 5	+10	(3·3)	+ 6·7		
	16	− 4·5	+10	(3)	+ 7		
	21	− 3·5	+ 9·5	(2·3)	+ 7·2		
993	0	+ 9·5	− 7	(6·3)	− 0·7	..	19
	5	+ 7·5	− 7	(5)	− 2		
		CO_2 for 1 minute					
	6	−15	+ 9·5	(10)	− 0·5		
	7	− 8	+ 3	(5·3)	− 2·3		
	8	−11	+ 5	(7·3)	− 2·3		
	9	−16·5	+10	(11)	− 1		
	10	−21	+14	(14)	0		
	15	−25	+26·5	(16·7)	+ 9·8		
	20	−15	+21	(10)	+11		
	25	− 7·5	+15·5	(5)	+10·5		
994	0	0	+ 9	(0)	+ 9	..	17·5
	3	0	+ 9	(0)	+ 9		
		Tetanisation, 10 units, 5 minutes					
		$\alpha = 0$			$\omega = +14$		
	9	− 3·5	+ 8	(2·3)	+ 5·7		
	13	− 3	+ 8	(2)	+ 6		
	18	− 2·5	+ 7·5	(1·7)	+ 5·8		
	23	− 2·5	+ 7	(1·7)	+ 5·3		
2003	0	− 7·5	+ 3	(5)	− 2	..	37
		Tetanisation, 10 units, 5 minutes					
		$\alpha = -8{\cdot}5$			$\omega = +5$		
	6	− 8·5	+ 3·5	(5·7)	− 2·2		
	20	− 9·5	+ 3	(6·3)	− 3·3		
2004	0	− 2·5	+10·5	(1·7)	+ 8·8		
	5	− 4	+11	(2·7)	+ 8·3		
		Tetanisation, 10 units, 5 minutes					
		$\alpha = -4{\cdot}5$			$\omega = +6{\cdot}5$		
	11	− 2·5	+ 2·5	(1·7)	+ 0·8		
	16	− 5	+12	(3·3)	+ 8·7		
	21	− 7	+11·5	(4·7)	+ 6·8		
	26	− 6·5	+11	(4·3)	+ 6·7		

TABLE D (continued).—Measurements of some of the Observations given in Tables B and C.

	Time.	I.	II.	(⅔ I.)	II. net.	I./II.	0·001 volt.
	minutes.						
2005	0	− 8	+15	(5·3)	+10·7		
	4	− 7	+17	(4·7)	+12·3		
		Tetanisation, 10 units, 5 minutes $\alpha = -7$ $\omega = +9{\cdot}5$					
	5	− 3·5	+ 4	(2·3)	+ 1·7		
	10	− 7·5	+15·5	(5)	+10·5		
	15	−10	+15	(6·7)	+ 8·3		
2006	0	− 4·5	+ 8	(3)	+ 5		
	5	− 4·5	+ 8	(3)	+ 5		
	10	− 4·5	+ 8	(3)	+ 5		
		CO_2 for 1 minute					
	11	−10	+ 6	(6·7)	− 0·7		
	12	− 4·5	+ 1	(3)	− 2		
	13	− 2·5	0	(1·7)	− 1·7		
	14	− 4·5	+ 1	(3)	− 2		
	15	− 6·5	+ 3·5	(4·3)	− 0·8		
	20	−10	+ 9	(6·7)	+ 2·3		
	28	− 7·5	+ 7	(5)	+ 2		
2054	0	− 8	+ 5	(5·3)	− 0·7	..	13
	5	−10·5	+ 5	(7)	− 2·0		
		Tetanisation, 10 units, 5 minutes $\alpha = -10{\cdot}5$ $\omega = +17$					
	11	−14·5	+ 5	(9·7)	− 4·7		
	20	−14	+ 4	(9·3)	− 5·3		
	28	−13·5	+ 4	(9)	− 5		
2055	0	−12	+ 4	(8)	− 4	..	15
	5	−12·5	+ 4	(8·3)	− 4·3		
		Tetanisation, 10 units, 5 minutes $\alpha = -12$ $\omega = +17$					
	11	−16·5	+ 4	(11)	− 7		
	20	−14·5	+ 3·5	(9·7)	− 6·2		
	27	−14	+ 2·5	(9·3)	− 6·8		
2057	0	− 5	+ 7	(3·3)	+ 3·7	..	16
	10	−12	+ 8	(8)	0		
		Tetanisation, 10 units, 5 minutes $\alpha = -11$ $\omega = +45$?					
	27	−23	+19	(15·3)	+ 3·7		
	30	−22	+17	(14·7)	+ 2·3		
	40	−18	+14	(12)	+ 2		
	50	−17	+13	(11·3)	+ 1·7		

TABLE D (continued).—Measurements of some of the Observations given in Tables B and C.

	Time.	I.	II.	(⅔ I.)	II. net.	I./II.	0·001 volt.
	minutes.						
2068	1	− 6	+14	(4)	+14	..	11
	10	− 8·5	+16	(5·7)	+11·3		
		Tetanisation, 10 units, 5 minutes					
	15	−16	+15	(10·7)	+ 4·3		
	25	−16	+14	(10·7)	+ 3·3		
		Tetanisation, 100 units, 5 minutes					
	30	− 3	+ 3·5	(2)	+ 1·5		
	40	− 7·5	+10	(5)	+ 5		
		Tetanisation, 10 units, 5 minutes					
	45	−19	+19	(12·7)	+ 6·3		
	55	−18	+18	(12)	+ 6		
		Tetanisation, 100 units, 5 minutes					
	60	− 1	+ 1·5	(0·7)	+ 0·8		
	70	− 2·5	+ 3·5	(1·7)	+ 1·8	..	8·5
2069	1	−10	+ 9	(6·7)	+ 2·3	..	21
	10	−12	+11	(8)	+ 3		
		Tetanisation, 10 units, 5 minutes					
	15	−20	+18	(13·3)	+ 4·7		
	25	−16·5	+14·5	(11)	+ 3·5		
		Tetanisation, 100 units, 5 minutes					
	30	− 3	+ 2·5	(2)	+ 0·5		
	40	− 6·5	+ 5·5	(4·3)	+ 1·2		
		Tetanisation, 10 units, 5 minutes					
	45	−14	+11·5	(9·3)	+ 2·2		
	55	−12	+10·5	(8)	+ 2·5		
		Tetanisation, 100 units, 5 minutes					
	60	0	0				
	70	0	0	..	..	..	19·5
2072	0	+ 1·5	+ 4	(1)	+ 5	..	15
		Tetanisation, 10 units, 5 minutes $\alpha = +1·5$ $\omega = +14$					
	6	− 3	+ 7	(2)	+ 5		
	10	0	+ 5·5	(0)	+ 5·5		
	15	0	+ 5	(0)	+ 5		
	20	+ 1	+ 4	(0·7)	+ 4·7		

TABLE D (continued).—Measurements of some of the Observations given in Tables B and C.

	Time.	I.	II.	(⅔ I.).	II. net.	I./II.	0·001 volt.
	minutes.						
2073	0	+ 7·5	+ 8·5	(5)	+13·5	..	30
	5	+ 7·5	+10·5	(5)	+13·5		
			CO₂ for 2 minutes				
	9	−16	0	(10·7)	−10·7		
	10	−17	?	(11·3)	?		
	20	−44	+44	(29·3)	+14·7	..	30
	27	−16	+26	(10·7)	+15·3		
2074	1	+ 3	+ 8·5	(2)	+10·5	..	19
	5	+ 1·5	+ 8·5	(1)	+ 9·5		
			Tetanisation, 10 units, 5 minutes $\alpha = +1·5$ $\omega = +18$				
	11	− 9·5	+11·5	(6·3)	+ 5·2		
	15	− 4·5	+ 8·5	(3)	+ 5·5		
	20	0	+ 7	(0)	+ 7		
2075	0	+ 5·5	+ 4	(3·7)	+ 7·7	..	19
	4	+ 6	+ 4	(4)	+ 8		
			CO₂ for 2 minutes				
	6	− 7	0	(4·7)	+ 4·7		
	10	−11	+ 4	(7·3)	+ 3·3		
	12	−23	+15·5	(15·3)	+ 0·2		
	15	−19·5	+17	(13)	+ 4·0		
	20	− 9	+11	(6)	+ 5		
	25	0	+ 5·5	(0)	+ 5·5	..	19
2080	0	− 3	+ 6	(2)	+ 4	..	12·5
	4	− 3·5	+ 5·5	(2·3)	+ 3·2		
			CO₂ for 2 minutes				
	7	−16·5	+ 9	(11)	− 2		
	10	−16·5	+ 9	(11)	− 2		
	12	−17·5	+12·5	(11·7)	+ 0·8		
	15	−12	+14	(8)	+ 6		
	20	− 8	+14	(5·3)	+ 8·7		
	25	− 6·5	+12	(4·3)	+ 7·7	..	12
2081	0	+ 5·5	− 4	(3·7)	− 0·3		
			Tetanisation, 10 units, 5 minutes				
	7	+10·5	− 3·5	(7)	+ 3·5		
	12	+ 8·5	− 4·5	(5·7)	+ 1·2		
	17	+ 8	− 5	(5·3)	+ 0·3		
	22	+ 7·5	− 5	(5)	0		

TABLE D (continued).—Measurements of some of the Observations given in Tables B and C.

	Time.	I.	II.	(⅔ I.).	II. net.	I./II.	0·001 volt.
2082	minutes. 0	+ 7·5	− 4·5	(5)	+ 0·5	..	18
	5	+ 6	− 5	(4)	− 1·0		
CO_2	6	− 8·5	+ 3·5	(5·7)	− 2·2		
	7	− 7·5	+ 2	(5)	− 3·0		
	8	− 5	+ 1·5	(3·3)	− 1·8		
	9	− 3	+ 1	(2)	− 1·0		
	10	− 3	+ 1	(2)	− 1·0		
	12	− 5	+ 3·5	(3·3)	+ 0·2		
	15	− 6·5	+10	(4·3)	+ 5·7		
	20	− 4	+ 5	(2·7)	+ 2·3		
2084	0	− 8·5	+ 6·5	5·7	+ 0·8		
	3	−10·5	+ 6	7	− 1		
		Tetanisation, 100 units, 5 minutes α = − 20·5 ω = + 15					
	10	?	?				
	15	− 2	+ 2	1·3	+ 0·7		
	20	− 4	+ 2·5	2·7	− 0·2		
	25	− 5·5	+ 3	3·7	− 0·7	..	13
2085	1	− 7·5	+10	(5·0)	+ 5	..	27
	4	− 8·0	+ 8·5	(5·3)	+ 3·2		
		Tetanisation, 10 units, 5 minutes α = ? ω = + 4·5					
	9	− 6·5	+ 3	(4·3)	− 1·3		
	15	− 9·0	+ 4·5	(6·0)	− 1·5		
	20	− 8·5	+ 5·5	(5·7)	− 0·2		
	25	− 7·5	+ 5·5	(5·0)	+ 0·5		
2241	1	− 2·5	0				
	2	− 2·5	0				
	3	− 2·5	0				
CO_2	4	− 5	0				
	5	−17	0				
	6	−22	+ 1				
	7	−25	+ 2				
	8	−26	+ 2·5				
	9	−24	+ 3·5				
	10	−20	+ 6				

TABLE D (continued).—Measurements of some of the Observations given in Tables B and C.

	Time.	I.	II.	($\frac{2}{3}$ I.)	II. net.	I./II.	0·001 volt.
	minutes.						
2242	1	− 6·5	+16			..	12
	2	− 5	+15				
	3	− 4·5	+14				
	4	−22	0				
	5	−19	0				
CO_2	6	−15	0				
	7	−12·5	0				
	8	−11	0				
	9	−11	0				
	10	−14	0				
	11	−18·5	0				
	12	−20	0				
	13	−21	+ 1·5				
	14	−18	+ 3				
	15	−14	+ 6·5				
	16	−10·5	+ 8·5				
	17	− 6	+11				
	18	− 4	+11				
	19	− 2·5	+10·5				
	20	− 1	+10				
	21	0	+ 9				

	Time.	I.	II.	(·6 I.)	II. net.	I./II.	0·001 volt.
	minutes.						
200	0	−10	+ 7	(6·0)	+ 1·0		
(fig. 14)	5	− 9·5	+ 7	(5·7)	+ 1·3		
	6	− 9·5	+ 6	(5·7)	+ 0·3		
	7	− 9	+ 4·5	(5·4)	− 0·9		
	8	0	0	(0)	0		
	9	0	0	(0)	0		
	10	− 6	+ 3	(3·6)	− 0·6		
	11	−14	+ 9	(8·4)	+ 0·6		
	12	−18	+13	(10·8)	+ 2·2		
	13	−19	+14·5	(11·4)	+ 3·1		
	14	−18	+14	(10·8)	+ 3·2		
	15	−16	+12·5	(9·6)	+ 2·9		
	20	−12·5	+ 9	(7·5)	+ 1·5		
	25	−11	+7·5	(6·6)	+ 0·9		

	Time.	I.	II.	($\frac{2}{3}$ I.)	II. net.	I./II.	0·001 volt.
	minutes.						
309	0	−11·5	+ 9·5	7·7	+ 1·8	..	10
(fig. 4)	5	−11	+ 9·3	7·3	+ 2		
	10	−10·5	+ 8·7	7	+ 1·7		
	15	10	8·3	6·7	+ 1·6		
	20	9·5	7·7	6·3	+ 1·4		
	25	9	7·5	6	+ 1·5		
	30	3·5	7·2	5·7	+ 1·5		
	35	8·3	6·8	5·5	+ 1·3		
	40	8	6·8	5·3	+ 1·5		

TABLE D (continued).—Measurements of some of the Observations given in Tables B and C.

	Time.	I.	II.	(⅔ I.)	II. net.	I./II.	0·001 volt.
	minutes.						
334	0	11·5	8·5	7·7	+ 0·8	..	16·5
(fig. 1)	5	11	8	7·3	+ 0·7		
	10	10·5	7·5	7	+ 0·5		
	15	10·5	7·5	7	+ 0·5		
	20	10	6·5	6·7	− 0·2		
	25	10	6	6·7	− 0·7	..	14·5
	Time.	I.	II.	(·6 I.)	II. net.	I./II.	0·001 volt.
	minutes.						
537	1	−14·5	+13·5	8·7			
(fig. 15)	2	−14·5	+13·5	8·7			
	3	−14·5	+13	8·7			
	4	−21	+23	12·6			
	5	−27·5	+14·5	16·8			
	6	−22	+10	13·2			
	7	−18·5	+ 9	11·0			
	8	−15·5	+ 8	9·6			
	9	−20	+11	12			
	10	−27	+16·5	16·2			
	11	−36	+23	21·6			
	17	−37	+33	22·3			
	21	−27	+27·5	16·2			
708	0	−17·5	+20	(10·5)	+ 9·5	..	20·5
(fig. 6)	10	−17·5	+21·5	(10·5)	+11·0		
	20	−17	+21·5	(10·2)	+11·3		
	30	−17	+21·5	(10·2)	+11·3		
	40	−17	+21·5	(10·2)	+11·3	..	17·5
2248	1	− 4	+ 1·5	..	..	..	11
	2	− 4	+ 1·5				
	3	−10	0				
	4	−13	0	} CO_2			
	5	−12	0				
	6	−12	0				
	7	−13	0				
	8	−18	0				
	9	−23					
	10	−27					
	11	−27					
	12	26	+ 2				
	13	24	+ 2·5				
	14	21	+ 3				
	15	18	+ 3				
	16	16	+ 3				
	17	14	+ 3				
	18	12	+ 3				
	19	10	+ 3				
	20	9	+ 3				

TABLE D (continued).—Measurements of some of the Observations given in Tables B and C.

	Time.	I.	II.	($\frac{3}{8}$ I.)	II. net.	I./II.	0·001 volt.
	minutes.						
2249	1	− 1	+ 0·5	..	..	..	11·5
	2	− 1	+ 0·5				
	3	− 1	+ 0·5				
	4	− 1	+ 0·5				
	5	− 1	+ 0·5				
	6	− 1	+ 0·5				
	7	− 6	..	} CO_2			
	8	− 7·5					
	9	− 8					
	10	− 9·5					
	11	−12					
	12	−14	+ 2·5				
	13	−13	+ 4				
	14	− 9·5	+ 7·5				
	15	− 7	+ 9				
	16	− 5·5	+10·5				
	17	− 5	+10·5				
	18	− 4·5	+ 9·5				
	19	− 4	+ 8·5				
	20	− 3·5	+ 7·5				
	25	− 2	+ 4	..	..	..	11·5
2251	0	− 8	+ 5	..	..	..	10·5
	5	− 8	+ 5				
			CO_2 for 1 minute				
	7	−20	0				
	8	−19	0				
	9	−22	0				
	10	−28	+ 2				
	11	−34	+ 6				
	12	−34	+ 6				
	13	−32	+ 7				
	14	−29	+ 7·5				
	15	−27	+ 8·5				
	20	−18	+8	.	..	..	10
	24	−13·5	+7				

Table D (continued).—Measurements of some of the Observations given in Tables B and C.

	Time.	I.	II.	($\frac{2}{5}$ I.)	II. net.	I./II.	0·001 volt.
	minutes.						
2256	0	− 6	+ 1	..	..	..	13·5
	5	− 6	+ 1				
	6	− 6	0				
	7	− 8	0	CO$_2$			
	8	− 5	0				
	9	− 5	0				
	10	− 8	0				
	11	−12	+ 1				
	12	−16	+ 1·5				
	13	−17	+ 2				
	14	−16	+ 2				
	15	− 5	+ 2				
	16	− 3·5	0	CO$_2$			
	17	− 2·5	0				
	18	− 4·5	0				
	19	− 8	0				
	20	−13	+ 1				
	21	−17	+ 1·5				
	22	−18	+ 2·5				
	23	−16·5	+ 3				
	24	−15	+ 3				
	25	−13·5	+ 3				
	26	−12	+ 2·5				
	27	− 10·5	+ 2·5				
	28	− 9·5	+ 2				
	29	− 8·5	+ 1·5				
	30	− 8	+ 1	..	..	..	13
2250	0	− 8·5	+ 3·5	..	..	..	11
	5	− 8·5	+ 2				
		Tetanisation, 10 units, 5 minutes $\alpha = -8·5$ $\omega = +12$					
	11	−10	+ 1				
	15	− 9	+ 1				
	20	− 8	+ 1				
	25	− 7	+ 1				
2258	0	− 3·5	+ 2·5	..	..	..	12·5
	5	− 3·5	+ 2·5				
		Tetanisation, 5 minutes $\alpha = -3·5$ $\omega = +8$					
	11	− 6	+ 1·5				
	15	− 5	+ 1·5				
	20	− 5	+ 1·5	..	..	..	11·5

TABLE D (continued).—Measurements of some of the Observations given in Tables B and C.

	Time.	I.	II.	(⅓ I.)	II. net.	I./II.	0·001 volt.
	minutes.						
2262	0	−15	+ 5				
	5	−15	+ 5				
			Tetanisation, 5 minutes $\alpha = -15$ $\omega = +26$				
	11	−22	+ 3·5				
	15	−20	+ 3·5				
	20	−19	+ 3·5				
2266	0	− 6	+ 4	..	..	..	7·5
	5	− 6	+ 3				
			Tetanisation, 5 minutes $\alpha = -6$ $\omega = +10$				
	11	− 9	+ 1·5				
	15	− 7	+ 2				
	20	− 6	+ 2	..	..	..	5·5
2268	0	− 2·5	+ 1·5	..	..	..	4·5
	4	− 2·5	+ 1·5				
			CO_2 for 2 minutes.				
	10	−11	+ 2				
	15	− 8	+ 3·5				
	20	− 5	+ 2·5	..	..	..	5
2271	0	−13	+ 3·5	..	..	..	14
	6	−15	+ 3·5				
			Tetanisation, 5 minutes $\alpha = -15$ $\omega = +29$				
	12	−23·5	+ 3				
	17	−20	+ 3·5				
	22	−18·5	+ 3·5	..	..	..	11
2274	0	− 6	+ 1·5	..	..	..	10
	5	− 6·5	+ 1·5				
			CO_2 for 1 minute				
	6	− 8	0				
	7	−14	+ 2				
	8	−17	+ 3				
	9	−19	+ 4				
	10	−20	+ 4·5				
	15	−17	+ 4				
	20	−12·5	+ 3				
	24	−11	+ 2	..	..	..	12

TABLE E.—Data relating to Chapter IV., § 4. Action of CO_2 on Polarising and Electrotonic Currents, &c.

Effect of Et_2O upon neg. var., upon anelectrotonus, and upon katelectrotonus.

Plate No.	Time.	Neg. var.	Anel.	Katel.	0·001 volt.
	mins.				
2154	1	−5	..	..	10
	2	..	+ 9·5	..	
	3	..	..	−4	
	4	−3	..	..	
	5	..	+ 9·5	..	
	6	..	..	−3·5	
		Ether vapour.			
	7	−3·5	..	..	
	8	..	+ 7·5	..	
	9	..	..	−3·5	
	10	..	..	..	
	11	..	+ 4	..	
	12	..	..	−4·5	
	13	..	..	..	
	14	..	+ 7	..	
	15	..	..	−5	
	16	−4	..	..	
	17	..	+ 9	..	
	18	..	..	−4·5	
	19	−0·5	..	..	
	20	..	+11	..	
	21	..	..	−4	
	22	+2	..	..	
	23	..	+11	..	
	24	..	..	−4	8·5

Effect of Et_2O on katelectrotonus.

Plate No.	Time.	S.	0·001 volt.
	minutes.		
2157	1	7·5	
	5	7·5	
	6	Ether vapour for 1 min.	
	7	10·5	
	8	12	
	9	..	
	10	12·5	
	11	..	
	12	..	
	13	..	
	14	..	
	15	8	
	20	6	
	25	6	12·5

Effect of CO_2 upon anelectrotonus and katelectrotonus.

Plate No.	Time.	Anel. N.	Katel. S.	0·001 volt.
	minutes.			
2158	1	19·5	..	15
	2	..	3	
	9	19·5	..	
	10	..	3	
		CO_2 for 3 mins.		
	13	8	..	
	14	..	3	
	15	8	..	
	16	..	3·5	
	17	17·5	..	
	18	..	5	
	19	24·5	..	
	20	..	6·5	
	21	24·5	..	
	22	..	7	
	23	24	..	
	24	..	5	
	25	24	..	
	26	..	4·5	

Effect of Aconitine upon anelectrotonus and upon katelectrotonus.

Plate No.		Anel.	Katel.	0·001 volt.
2159	Before aconitine .	+15·0	−5·5	
	After aconitine .	+ 4·0	−4·0	
	After interpolar crush	+ 4·0	−4·0	

Table E (continued).—Data relating to Chapter IV., § 4.

Effect of Et_2O on katelectrotonus.

Plate No.	Time.	S.	0·001 volt.
2168	minutes. 1	12·5	13·5
	5	11·5	
	6	6·0	Ether vapour for 3 mins.
	7	3·0	
	8	3·0	
	9	3·0	
	10	3·5	
	11	3·5	
	12	4·0	
	13	4·0	
	14	4·5	
	15	5·0	
	20	6·5	
	25	7·0	12·5

Effect of Et_2O on anelectrotonus.

Plate No.	Time.	N.	0·001 volt.
2169 (fig. 68)	minutes. 1	10·5	13
	5	10·5	
	6	10·5	Ether vapour for 3 mins.
	7	4·0	
	8	3·0	
	9	2·0	
	10	2·5	
	11	3·0	
	12	3·0	
	13	3·5	
	14	4·0	
	15	4·0	
	20	8·5	
	25	11·5	
	30	12·5	12

Effect of Et_2O on anelectrotonus.

Plate No.	Time.	I. N. effect.	II. S. after-effect.	0·001 volt.
2170	minutes. 1	11·0	5·5	15
	5	11·0	5·0	
	6	10·5	Ether vapour for 4 mins.	
	7	4·0		
	8	2·5		
	9	2·0		
	10	2·0	0	
	11	3·0	0	
	12	3·5	0	
	13	3·5	0	
	14	3·5	0	
	15	4·0	0	
	20	6·0	0	
	25	8·5	0	
	30	10·5	0	14·5

Effect of $CHCl_3$ on anelectrotonus.

Plate No.	Time.	N.	0·001 volt.
2171	minutes. 1	11·0	14
	5	11·0	
	6	15·5	
	7	13·0	
	8	9·5	
	9	..	
	10	4·5	
	11	3·0	
	12	2·0	
	13	2·0	
	14	2·0	
	15	2·0	
	20	1·0	
	25	0·5	
	30	0·5	14

TABLE E (continued).—Data relating to Chapter IV., § 4.

Effect of CO_2 on neg. var. of katelectrotonus.

Plate No.	Time.		0·001 volt.
	minutes.		
2181 (fig. 51)	1	N. 15·5	20
	5	„ 14·5	
	6	CO_2 for 1 min.	
	7	S. 6·0	
	8	„ 5·0	
	9	„ 4·5	
	10	„ 3·5	
	11	„ 3·5	
	12	N. 4·0	
	13	„ 6·0	
	14	„ 8·5	
	15	„ 10·0	
	20	„ 11·0	19

Effect of CO_2 on neg. var. of anelectrotonus.

Plate No.	Time.	S.	0·001 volt.
	minutes.		
2182	1	22	
	5	29	
	6	CO_2 for 1 min.	
	7	24	
	8	27	
	9	30	
	10	34	
	15	35	
	20	35	15

Effect of CO_2 on neg. var. of anelectrotonus.

Plate No.	Time.	S.	0·001 volt.
	minutes.		
2185 (fig. 52)	1	12·5	19
	5	19·0	
	6	CO_2 for 1 min.	
	7	13·0	
	8	10·0	
	9	12·0	
	10	16·5	
	15	21·0	
	20	22·0	17·5

Effect of CO_2 on neg. var. of anelectrotonus.

Plate No.	Time.	S.	0·001 volt.
	minutes.		
2190	1	27·0	17
	5	27·0	
	6	CO_2 for 1 min.	
	7	24·5	
	8	28·0	
	9	30·0	
	10	31·0	
	11	30·0	
	12	29·5	
	13	27·5	
	14	26·5	
	15	25·0	
	16	24·0	
	17	23·5	
	18	23·0	

Effect of CO_2 on anelectrotonus.

Plate No.	Time.	N.	0·001 volt.
	minutes.		
2192	1	43·5	16·5
	5	44	
	6	CO_2 for 1 min.	
	7	30	
	8	35	
	9	39	
	10	Off plate	
	15	55	
	20	57	

Effect of CO_2 on anelectrotonus.

Plate No.	Time.	N.	0·001 volt.
	minutes.		
2194	1	22	22
	5	25	
	6	CO_2 for 1 min.	
	7	14	
	8	17	
	9	19	
	10	Off plate	
	15	„	
	20	37·5	21

TABLE E (continued).—Data relating to Chapter IV., § 4.

Effect of CO$_2$ on katelectrotonus.

Plate No.	Time. minutes.	S.	0·001 volt.
2195 (fig. 49)	1	12	19
	5	12·5	
	6	CO$_2$ for 1 min.	
	7	17·5	
	8	16·5	
	9	18·5	
	10	23·0	
	11	26·5	
	12	28·5	
	13	27·0	
	14	25·0	
	15	23·0	
	20	18·0	
	25	15·0	19

Effect of CO$_2$ on anelectrotonus.

Plate No.	Time. minutes.	N.	0·001 volt.
2196 (fig. 50)	1	26·0	
	5	26·0	
	6	CO$_2$ for 1 min.	
	7	15·0	
	8	20·0	
	9	22·0	
	10	24·0	
	15	38·5	
	20	36·5	
	25	33·0	18

Effect of CO$_2$ on katelectrotonus.

Plate No.	Time. minutes.	S.	0·001 volt.
2197	1	11·5	18·5
	5	11·5	
	6	CO$_2$ for 1 min.	
	7	13·5	
	8	14·0	
	9	16·5	
	10	21·0	
	11	26·0	
	12	27·0	
	13	25·0	
	14	22·5	
	15	20·5	
	20	16·5	18

Effect of CO$_2$ on anelectrotonus.

Plate No.	Time. minutes.	N.	0·001 volt.
2198	1	29	24
	5	30	
	6	CO$_2$ for 1 min.	
	7	19	
	8	22	
	9	24	
	10	27	
	15	Off plate	
	20	36	

Effect of CO$_2$ on anelectrotonus.

Plate No.	Time. minutes.	N.	0·001 volt.
2199	0	6·5	7·5
	5	7·0	
	6	10·0	} CO$_2$
	7	13·5	
	8	14·0	
	9	14·5	
	10	15·0	
	15	12·5	
	20	9·5	
	25	8·5	
	30	7·5	7·0

Effect of CO$_2$ on anelectrotonus.

Plate No.	Time. minutes.	N.	0·001 volt.
2200	1	21·0	
	5	21·0	
	6	CO$_2$ for 1 min.	
	7	9·5	
	8	11·5	
	9	13·0	
	10	15·0	
	11	17·0	
	12	19·0	
	13	21·0	
	14	22·0	
	15	23·0	

TABLE E (continued).—Data relating to Chapter IV., § 4.

Effect of aconitine on neg. var., on anel., and on katel.

Plate No.	Time.	Neg. var.	Anel.	Katel.	0·001 volt.
	mins.				
2201	1	−9	..	..	11·5
	2	..	+14	..	
	3	..	..	−4·5	
	4	−8	..	..	
	5	..	+14	..	
	6	..	..	−4·0	
	7	−7	..	..	
	8	..	+14	..	
	9	..	..	−4·0	
	Bath of Aconitine Hydrochloride 1 per cent. for 1 minute.				
	14	−5·5	..	..	11·0
	15	..	+ 9·0	..	
	16	..	..	−2·5	
	17	−4.5	..	..	
	18	..	+ 5·5	..	
	19	..	..	−2·5	
	20	−0·5	..	..	
	21	..	+ 4·0	..	
	22	..	..	−2·5	
	23	0·0	..	..	
	24	..	+ 2·5	..	
	25	..	..	−2·5	11·5
	26	Nerve crushed in interpolar region			
	27	0·0	..	..	
	28	..	0·0	..	
	29	..	..	0·0	11

Effect of CO_2 on N. polarisation increment.

Plate No.	Time.	N.	0·001 volt.
	minutes.		
2203 (fig. 56)	1	17·5	13·5
	5	18·5	
	6	CO_2 for 1 min.	
	7	4·5	
	8	9·0	
	9	7·5	
	10	5·0	
	11	5·5	
	12	9·5	
	13	14·0	
	14	16·5	
	15	18·5	
	20	22·5	
	25	23·5	13·5

Effect of CO_2 on S. polarisation increment.

Plate No.	Time.	S.	0·001 volt.
	minutes.		
2204 (fig. 55)	1	13·0	12
	5	13·0	
	6	CO_2 for 1 min.	
	7	12·0	
	8	8·0	
	9	9·0	
	10	11·5	
	11	15·5	
	12	19·5	
	13	21·5	
	14	23·5	
	15	23·5	
	20	20·5	
	25	18·5	12·5

Effect of CO_2 on S. polarisation increment.

Plate No.	Time.	S.	0·001 volt.
	minutes.		
2205	1	12·0	12
	5	12·0	
	6	CO_2 for 1 min.	
	7	8·0	
	8	7·0	
	9	..	
	10	10·5	
	15	18·5	
	20	17·0	11·5

Effect of CO_2 on N. polarisation increment.

Plate No.	Time.	N.	0·001 volt.
	minutes.		
2206	1	17·0	12·5
	5	16·5	
	6	CO_2 for 1 min.	
	7	..	
	8	5·0	
	9	6·5	
	10	8·0	
	15	17·5	
	20	18·5	12·5

TABLE E (continued).—Data relating to Chapter IV., § 4.

Effect of CO_2 on polarising current.

Plate No.	Time.	S.	0·001 volt.
	minutes.		
2207 (fig. 53)	1	19·5	17
	5	19·5	
	6	CO_2 for 2 min.	
	7	19·5	
	8	19·5	
	9	19·5	
	10	19·5	
	15	19·5	
	20	19·5	17
		N.	
2208 (fig. 54)	1	19·5	17
	5	19.5	
	6	CO_2 for 2 min.	
	7	19·5	
	8	19·5	
	9	19·5	
	10	19·5	
	15	19·5	
	20	19·5	17

Effect of $CHCl_3$ on neg. var., on anelectrotonus, and on katelectrotonus.

Plate No.	Time.	Neg. var.	Anel.	Katel.	0·001 volt.
	mins.				
2211	1	−8	..	..	12
	2	..	+11	..	
	3	..	..	−5	
	4	−7	..	..	
	5	..	+ 9	..	
	6	..	..	−4·5	
	7	−7	..	..	
	8	..	+10	..	
	9	..	..	−5	
	10 11	Chloroform vapour			
	15	0	..	..	
	16	..	+ 1	..	
	17	..	..	−1	
	30	0	..	..	
	31	..	+ 1	..	
	32	..	..	−1	

Effect of Et_2O on neg. var. of anelectrotonus.

Plate No.	Time.	S.	0·001 volt.
	minutes.		
2209	1	33	13
	5	33	
	6	39	Ether vapour for 2 mins.
	7	24	
	8	11	
	9	11	
	10	9	
	11	13	
	12	17	
	13	22	
	14	26	
	15	30	
	16	32	
	17	33	
	18	34	
	19	34	13

Effect of Et_2O on katelectrotonus.

Plate No.	Time.	S.	0·001 volt.
	minutes.		
2220	1	24·0	9
	5	24·5	
	6	27·0	Ether vapour for 2 mins.
	7	30·5	
	8	29·5	
	9	33·0	
	10	34·5	
	11	36·0	
	12	37·0	
	13	37·5	
	14	37·0	
	15	36·0	
	20	31·0	
	25	26·5	

TABLE E (continued).—Data relating to Chapter IV., § 4.

Effect of Et_2O on anelectrotonus.

Plate No.	Time.	N.	0·001 volt.
2221	minutes. 1	52·0	10
	5	54·0	
	6	..	Ether vapour for 2 mins.
	7	42·0	
	8	41·0	
	9	42·0	
	10	44·0	
	11	45·5	
	12	47·0	
	13	48·0	
	14	49·5	
	15	50·0	
	20	51·0	
	25	51·5	10

Effect of Et_2O on S. polarisation increment.

Plate No.	Time.	S.	0·001 volt.
2223	minutes. 1	27·0	12·5
	5	27·0	
	6	..	Ether vapour for 2 mins.
	7	..	
	8	..	
	9	0·0	
	10	0·0	
	11	1·0	
	12	6·5	
	13	18·0	
	14	..	
	15	24·5	
	20	23·0	12

Effect of Et_2O on N. polarisation increment.

Plate No.	Time.		0·001 volt.
2224	minutes. 1	N. 20·0	
	5	„ 18·5	
	6	„ ..	Ether vapour for 2 mins.
	7	„ ..	
	8	„ ..	
	9	„ 0·0	
	10	„ 0·0	
	11	S. 1·0	
	12	„ 3·0	
	13	„ 10·0	
	14	„ 11·0	
	15	„ 6·0	
	16	N. 1·5	
	17	„ 4·5	
	18	„ 7·0	
	19	„ 8·0	
	20	„ 10·0	
	21	„ 11·0	
	22	„ 11·5	11

Effect of Et_2O on S. polarisation increment.

Plate No.	Time.	S.	0·001 volt.
2225	minutes. 1	12·0	13
	5	12	
	6	..	Ether vapour for 2 mins.
	7	..	
	8	0·0	
	9	0·0	
	10	0·0	
	11	1·0	
	12	1·0	
	13	3·0	
	14	11·0	
	15	15·5	
	20	16·0	13

TABLE E (continued).—Data relating to Chapter IV., § 4.

Effect of $CHCl_3$ on S. polarisation increment.

Plate No.	Time.	S.	0·001 volt.
	minutes.		
2226	1	13·0	11·5
	5	13·0	
	6	6·0	Chloroform vapour for 2 mins.
	7	2·0	
	8	0·0	
	9	0·0	
	10	0·0	
	11	0·0	
	12	0·0	
	13	0·0	
	14	0·0	
	15	0·5	
	20	1·5	

Effect of Et_2O on N. polarisation increment.

Plate No.	Time.		0·001 volt.
	minutes.		
2227	1	N. 14·0	14
	2	„ 14·0	
	3	„ 14·0	
	4	„ 14·0	
	5	„ 14·0	
	6	„ ..	Ether vapour for 2 mins.
	7	„ ..	
	8	„ ..	
	9	S. 2·5	
	10	„ 2·5	
	11	„ 1·5	
	12	N. 6·0	
	13	„ 9·5	
	14	„ 12·0	
	15	„ 12·5	
	20	„ 13·5	13·5

Effect of $CHCl_3$ on N. polarisation increment.

Plate No.	Time.	N.	0·001 volt.
	minutes.		
2228	1	14·5	13·5
	5	14·5	
	6	0·0	Chloroform vapour for 2 mins.
	7	0·0	
	10	0·0	
	15	0·0	
	20	0·0	13·5

Effect of $CHCl_3$ on anelectrotonus.

Plate No.	Time.	N.	0·001 volt.
	minutes.		
2231	1	24·5	15
	5	25·0	
	6	24·0	Chloroform vapour for 2 mins.
	7	16·0	
	8	9·5	
	9	8·5	
	10	9·0	
	15	6·0	
	20	5·5	
	25	5·5	15

Effect of $CHCl_3$ on katelectrotonus.

Plate No.	Time.	S.	0·001 volt.
	minutes.		
2232	1	6·5	6·5
	5	6·5	
	6	..	Chloroform vapour for 2 mins.
	7	6·0	
	8	6·0	
	9	5·0	
	10	4·5	
	15	2·5	
	20	1·5	
	25	1·5	7

TABLE E (continued).—Data relating to Chapter IV., § 4.

Effect of Et_2O on katelectrotonus.

Plate No.	Time.	S.	0·000 volt.
2233	minutes. 0	10·5	11
	5	10·5	
	6	11·0	Et_2O
	7	10·0	
	8	..	
	9	9·0	
	15	7·0	
	20	6·5	
	25	5·5	
	30	5·0	11

Effect of CO_2 on neg. var., on anelectrotonus, and on katelectrotonus.

Plate No.	Time.	Neg. var.	Auel.	Katel.	0·001 volt.
2235	mins. 1	− 3·5	..	..	9·5
	2	..	+ 7·5	..	
	3	..	..	−1·5	
			CO_2 for 1 min.		
	5	7·5	..	..	
	6	..	2·5	..	
	7	..	..	1·5	
	8	10·5	..	..	
	9	..	7·0	..	
	10	..	..	7·0	
	11	4	..	..	
	12	..	18·0	..	
	13	..	..	2·5	
	14	1·5	..	..	
	15	..	14·5	..	
	16	..	..	4·0	
	17	2·5	..	..	
	18	..	9·5	..	
	19	..	..	4·5	
	20	2	..	..	
	21	..	+ 8	..	
	22	..	..	−4	
	23	− 2	..	..	
	24	..	+ 7	..	
	25	..	..	−4	

Effect of CO_2 on neg. var.; on anelectrotonus and on katelectrotonus.

Plate No.		Neg. var.	Anel.	Katel.	0·001 volt.
2236	Before CO_2 .	−4	+9·5	−4·5	10
	10 minutes after CO_2	−9	+12	−7·5	

All deflections abolished by crushing the nerve between exciting and leading-off electrodes.

Effect of $CHCl_3$ on neg. var. of katelectrotonus.

Plate No.	Time.	N.	0·001 volt.
2237	minutes. 1	20	13·5
	5	18	
	6	0	Chloroform vapour for 2 min.
	7	0	
	8	0	
	9	0	
	10	0	
	15	0	
	20	0	
	25	0	14·5

Effect of $CHCl_3$ on anelectrotonus.

Plate No.	Time.	N.	0·001 volt.
2239	minutes. 0	9·5	9·0
	5	9·5	
	6	9·0	
	7	3·5	
	8	..	
	9	3·5	
	10	..	
	11	3·5	
	16	3·5	
	21	3·5	
	29	3·5	10·5

This deflection persisted after the nerve had been completely crushed between the exciting and leading-off electrodes.

TABLE E (continued).—Data relating to Chapter IV., § 4.

Effect of Et_2O on anelectrotonus and katelectrotonus.

Plate No.	Time.	Anel.	Katel.	0·001 volt.
		minutes.		
2288–9	1	+8·5	..	10
	2	..	−2·0	
	3	+8·5	..	
	4	..	−2·5	
	5	+8·5	..	
	6	..	−2·5	
	7	+9·0	..	
	8	..	..	
	Ether vapour for 2 mins.			
	15	+1·5	..	
	16	..	−1·5	
	25	+1·0	..	
	26	..	−0·5	
	33	+1·5	..	
	34	..	−0·5	10
	Pause of 30 mins.			
	64	+5 5	..	9
	65	..	−2·5	
	66	+5·5	..	
	67	..	−2·5	
	68	+5·5	..	
	69	..	−2·5	
	Ether vapour for 2 mins.			
	72	+trace	..	
	73	..	−trace	
	78	+trace	..	
	79	..	−trace	
	Nerve crushed in interpolar region.			
	81	+trace	..	
	82	..	−trace	

Effect of ether on neg. var., on anel., and on katel.

Plate No.	Time.	Neg. var.	Anel.	Katel.	0·001 volt.
	mins.				
2290	1	−10·5	..	..	12
	2	..	+10	..	
	3	..	..	−1·5	
	4	−10	..	..	
	5	..	+ 9	..	
	6	..	..	−1·5	
	7	−10	..	..	
	8	..	..	..	
	9	..	..	−1·5	
		Ether vapour for 3 minutes			
	13	0·0	..	..	
	14	..	+ 4·5	..	
	15	..	..	−1	
	16	0·0	..	..	
	17	..	+ 4·5	..	
	18	..	..	−1	
	19	0·0	..	..	
	20	..	+ 3·5	..	
	21	..	..	−1	
	22	0·0	..	..	
	23	..	+ 3	..	
	24	..	..	−1	
	25	0·0	..	..	
	26	..	+ 2	..	
	27	..	..	−0·5	12·5
		Nerve crushed in interpolar region			
	31	0·0	..	..	
	32	..	0·0	..	
	33	..	..	0·0	12

TABLE E (continued).—Data relating to Chapter IV., § 4.

Effect of Et_2O on anelectrotonus and katelectrotonus.

Plate No.	Time.	Anel.	Katel.	0·001 volt.
	minutes.			
2291	1	+31	..	12·5
	2	..	−6	
	3	+31	..	
	4	..	−5·5	
	5	+31	..	
	6	..	−6	
	7	+29·5	..	
	8	..	−5·5	
	9	+29·5	..	
	10	..	−5·5	
		Ether vapour		
	11	+ 9·5	..	
	12	..	−6	
	13	+ 5	..	
	14	..	−5	
	15	+ 6	..	
	16	..	−4·5	
	17	+ 6	..	
	18	..	−4	
	19	+ 5	..	
	20	..	−3	
	21	+ 5	..	
	22	..	−3	
	23	+ 4	..	
	24	..	−2	
	25	+ 4	..	12·5
		Nerve crushed in interpolar region		
	27	..	− trace	
	28	+ trace	..	
	29	..	− trace	
	30	+ trace	..	12

Effect of ether on anelectrotonus.

Plate No.	Time.			0·001 volt.
	minutes.			
2292	1	+35		13
	5	+35		
	10	+36		
	11	+35		
	12	+18	} Ether vapour	
	13	+10·5		
	14	+10·5		
	15	+ 8		
	16	+ 7		
	17	+ 6·5		
	18	+ 6		
	19	+ 6		
	20	+ 6		
	25	+ 4·5		
	30	+ 4		
	35	+ 3		
	40	+ 3		
	45	+ 3		12·5

No deflection after interpolar crush.

Effect of ether on neg. var. and on anelectrotonus.

Plate No.	Time.	Neg. var.	Anel.	0·001 volt.
	mins.			
2293	1	−6·5	..	14·0
	2	..	+17·0	
	9	−7·5	..	
	10	..	+18·0	
		Ether vapour for 4 minutes.		
	15	0·0	..	
	16	..	+ 6·0	
	23	0·0	..	
	24	..	+ 4·0	
	29	0·0	..	
	30	..	+ 3·5	
	35	0·0	..	
	36	..	+ 4·0	
	41	0·0	..	
	42	..	+ 4·5	12·5

No deflection after interpolar crush.

TABLE E (continued).—Data relating to Chapter IV., § 3.

Effect of tetanisation upon katelectrotonus.

Plate No.	Time.		0·001 volt.
	minutes.		
2294	0	+8·5	12·5
	2	−8·5	
	4	−8·5	
	6	−8·5	
		Tetanisation, 30 units, 5 mins.	
	14	−9·5	
	16	−9·0	
	18	−9·0	
	20	−9·0	
	22	−9·0	
	24	−9·0	
	26	−9·0	

Effect of tetanisation upon anelectrotonus.

Plate No.	Time.		0·001 volt.
	minutes.		
2296	0	+18·0	9
	5	+19·0	
	10	+19·0	
		Tetanisation, 50 units, 5 mins.	
	18	+12·0	
	19	+12·5	
	20	+13·0	
	25	+14·0	
	30	+14·5	
		Nerve crushed in interpolar region.	
	32	+ 2·5	

Effect of tetanisation upon anelectrotonus.

Plate No.	Time.		0·001 volt.
	minutes.		
2295	0	+30·5	
	2	+30·5	
	4	+30·0	
	6	+31·5	
		Tetanisation, 50 units, 5 mins.	
	13	+34·5	
	15	+34·5	
	17	+34·0	
	19	+33·0	
	21	+32·5	
	23	+32·0	

F.—TIME TABLE.

In view of possible differences in nerve-reaction with season, the following Time Table is added, by reference to which the date of any given observation may be approximately determined.

Plate No.	1,	January	3,	1895.
,, ,,	50,	February	1,	,,
,, ,,	100,	,,	25,	,,
,, ,,	150,	March	6,	,,
,, ,,	200,	July	6,	,,
,, ,,	250,	,,	16,	,,
,, ,,	300,	,,	25,	,,
,, ,,	350,	August	4,	,,
,, ,,	400,	,,	12,	,,
,, ,,	450,	,,	20,	,,
,, ,,	500,	,,	26,	,,
,, ,,	550,	October	5,	,,
,, ,,	600,	,,	13,	,,
,, ,,	650,	,,	22,	,,
,, ,,	700,	November	2,	,,
,, ,,	750,	,,	9,	,,
,, ,,	800,	,,	21,	,,
Plate No.	850,	November	28,	1895.
,, ,,	900,	December	5,	,,
,, ,,	950,	,,	13,	,,
,, ,,	1000,	January	3,	1896.
,, ,,	2000,	,,	,,	,,
,, ,,	2050,	,,	10,	,,
,, ,,	2100,	,,	21,	,,
,, ,,	2150,	February	3,	,,
,, ,,	2200,	,,	13,	,,
,, ,,	2250,	March	6,	,,
,, ,,	2250 to 2300,	July,		,,
,, ,,	3000,	May	10,	,,
,, ,,	3050,	June	2,	,,
,, ,,	3100,	,,	16,	,,
,, ,,	3150,	July	1,	,,
,, ,,	3200,	,,	18,	,,

NOTE.—Several points referred to in the lecture as delivered, in order to justify the extended and systematic application of the method to chemico-physiological questions, and mentioned therefore in the lecture-abstract ('Roy. Soc. Proc.,' March 12, 1896), have not been discussed in the foregoing paper, the principal theme of which is constituted by the discussion of the relations of carbon dioxide to the electrical reactions of medullated nerve. These points (action of anæsthetics, of acids, bases and salts, of alkaloids and narcotics, of aconitine and its constituents, &c.) will be presented *in extenso* in further papers. The action of anæsthetics is considered in some detail in the current number of 'Brain,' June, 1896.)

I desire to make some slight acknowledgment of the help that I have received from Miss S. C. M. SOWTON, in carrying out experiments. The undivided attention and great neatness with which Miss SOWTON has worked have furnished me with a much larger body of useful data than I could otherwise have obtained. Many of the most successful records have been obtained for me in my absence.

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II. *Phenomena resulting from Interruption of Afferent and Efferent Tracts of the Cerebellum.*

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Communicated by Professor Victor Horsley, *F.R.S.*

(From the Pathological Laboratory of University College, London.)

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1. Introduction.

I am greatly indebted to Professor Victor Horsley for allowing me to carry out the investigations, the results of which are embodied in this paper, in the Pathological Laboratory of University College, London.

My object in undertaking this research, was twofold, as I wished in the first place to obtain evidence in support of or against the view that the cerebellum exercises a direct influence on the spinal centres, as opposed to any indirect influence exerted through the agency of the cerebral cortex, and in the second place to ascertain whether any descending tract could be traced from the cerebellum, by way of which any such direct influence could be brought to bear on the spinal centres. It is, however, impossible for me to do more than deal with the first of these problems in the present paper.

In a former paper, dealing with ablation experiments on the cerebellum, I showed that while some of the effects obtained might result from the altered excitability of the cerebral cortex, which was demonstrated to exist, it was impossible to avoid the conclusion that others were the result of the removal of a direct influence which the cerebellar centres normally exerted over those of the spinal cord. The best way to obtain positive evidence on this point appeared to be to divide the inferior cerebellar peduncle on one side, leaving the organ itself and its other peduncles otherwise intact; this has accordingly been done; and the results obtained form part of the present communication. It however quickly became apparent that to perform this operation without injury to the auditory nuclei, and without including some fibres of the superior peduncle in the lesion, was no easy task.

It seemed desirable, as a control, to ascertain whether the effects obtained on section of the inferior cerebellar peduncle were also to be obtained when a section of the lateral region of the medulla was made between the posterior column nuclei and olive, so as to interrupt the direct cerebellar and lateral medullary tracts, without implicating the posterior columns or their nuclei; and these results have been in their turn controlled by experiments in which a transverse section was made, including the posterior columns and their nuclei on one side a few millimetres above the level of the calamus scriptorius.

Further control experiments consisted in performing almost complete hemisection of the medulla about 3 or 4 millims. above the calamus scriptorius, the pyramid being alone excluded from the section. The knife entering the medulla from the middle line posteriorly was made to pass through the organ in such a way as to divide all structures on one side with the exception of the pyramid. In other instances, the olive was excluded from the section also, the knife entering in the middle line from behind, as in the last case, but being brought out at the lateral region by the medulla just dorsal to the region of the olive.

2. Historical Review.

Numerous as have been the experimental investigations into the functions of the cerebellum, the middle are the only peduncles of the organ to which attention has specially been directed by any number of experimental physiologists. Very few observers have made the inferior peduncle the subject of separate investigation.

LABORDE* found that injuries of the restiform tracts caused disorders of equilibration similar to those caused by lesions of the semicircular canals.

FERRIER and TURNER† destroyed the left inferior peduncle in one monkey by the galvano-cautery, and divided it in four others, after which there was incurvation of the vertebral axis to the left. The left limbs were adducted and flexed, and the right extended and abducted. Attempts at movement occasioned rolling from right to left. Knee-jerks were equal and normal. There was no loss of sensibility. No ocular deviation was present, except in one case, but in two of the animals there were nystagmoid movements of the globes.

BIEDL‡ divided the restiform body and ascending root of the fifth nerve on the left side in cats, and found that no paralysis resulted, but that there were marked disturbances of co-ordination in the extremities on the side of the lesion and in the head and neck muscles.

3. PLAN OF EXPERIMENTATION.

I. Division of the Inferior Cerebellar Peduncle on one side.
II. Partial Section of the Lateral Region of the Medulla on one side (control).
III. Transverse Section of the Posterior Columns and their Nuclei on one side, a few millimetres above the Calamus Scriptorius (control).
IV. Comparison by the Electrical Excitability of the two Cerebral Hemispheres—
    (A.) One Inferior Cerebellar Peduncle divided;
    (B.) Partial Hemisection of the Medulla.
V. General convulsions induced by Intravenous Injection of Absinthe—
    (A.) One Inferior Cerebellar Peduncle divided;
    (B.) Partial Hemisection of the Medulla;
    (C.) Transverse Section of the Posterior Columns and their Nuclei on one side.

4. OPERATIVE PROCEDURE.

In all the experiments, the animals were first placed under the anæsthetic influence of ether, which was administered by inhalation, and the narcosis was continued until the end of the experiment, when the animal was killed under its influence. In those cases in which it was necessary to allow the animal to live after the operation, and where there was any likelihood of any pain resulting, morphia was administered, by subcutaneous injection, before the anæsthetic influence of the ether had passed off. Such animals were killed under the influence of ether at the end of the time that it was necessary to observe the symptoms resulting from the lesion. Tracheotomy was performed in all cases where it was not intended to allow the animal to live after the subsequent operative and other procedures. The external jugular vein was exposed on one side of the neck in those instances where absinthe was to be administered.

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* LABORDE, 'Compt. Rend. de la Soc. de Biol.,' 1882, p. 427.

† FERRIER and TURNER, 'Phil. Trans., Roy. Soc.,' 1894, p. 749.

‡ BIEDL, 'Wiener Klin. Woch.,' 1894, Nr. 46.

A single longitudinal incision was made in the middle line at the back of the head and neck, and the muscles cut and scraped away from their attachments to the occipital bone and upper cervical spines. The muscles were divided and scraped away as equally as possible on the two sides, so as to exclude the possibility of any rotation or twisting of the head in some direction being due to the action of muscles having their attachments intact on one side, while the corresponding muscles of the opposite side had been separated from their attachments. Bone forceps were alone used to effect an opening into the cranial cavity and neural canal, and after opening the theca the posterior part of the cerebellum was carefully separated from the medulla oblongata and raised to the extent necessary for the performance of the section of the inferior peduncle of the cerebellum as it enters the organ, or for the division of the posterior columns and their nuclei, and the tracts which occupy the lateral region of the medulla, or to perform partial hemisection of the medulla. In those instances in which a section of the lateral region of the medulla was made it was further necessary to make gentle traction on the medulla so as to displace it slightly to the opposite side in order to allow of the possibility of accurately delimiting the extent of the lesion. The actual section of any part was made by means of a narrow-bladed delicate knife.

When it was necessary to expose the cerebral cortex an opening was effected into the cranial cavity, at some point away from the motor areas for the limbs, by means of a small trephine, and the opening was subsequently enlarged by means of bone forceps. Every possible precaution was taken to avoid injury to the cortex, and the two hemispheres were treated exactly alike, so as to place them in precisely the same condition; they were kept warm and irrigated with warm normal salt solution throughout the excitation experiments.

In every instance in which it was intended that the animal should be allowed to survive the operation, this was done under the strictest possible antiseptic precautions. The skin was first shaved, thoroughly cleansed by soap and water, and afterwards well scrubbed with perchloride of mercury lotion (1–1000). The same strength of lotion was used for sponging out the wound during the operation until the stage at which the dura mater was about to be opened was reached, from which point boiled normal salt solution was alone used, so as to exclude the possibility of any myelitic complication arising from the action of the antiseptic lotion on the nerve structures. At the termination of the operation the external wound was once more sponged out with perchloride of mercury lotion, and then the whole washed carefully with normal salt solution. The edges of the skin wound were brought together by aseptic horsehair sutures, a small opening being left at the most dependent part for drainage, the surface of the skin again washed with perchloride of mercury lotion, and an antiseptic dressing applied.

When absinthe was used with a view to evoke convulsions in the animal, three to six minim doses of the essential oil were injected into the blood stream by way of the external jugular vein.

Electrical excitation of the cerebrum was effected by means of fine closely approximated platinum-pointed electrodes attached to the secondary coil of a Du Bois-Reymond's inductorium supplied by a single bichromate cell.

The records of muscular contractions were taken, in the case of the anterior extremities, from the extensor muscles of the wrist and digits, while in the case of the posterior extremities they were taken from the sural muscles. In either case the muscles and tendons were freely separated from the bones and other underlying structures to a considerable longitudinal extent, and the tendons of the two limbs attached to two Fick's spring myographs whose springs were as nearly as possible of equal strength. The writing points of these were of the same length, and were made to record on the blackened surface of paper stretched between two revolving cylinders kept in motion by means of a clock.

5. The Effect of Division of One Inferior Cerebellar Peduncle.*

In these experiments the peduncle was always divided as high up as possible, as it enters the cerebellum, in the hope that the fibres contained in the peduncle might alone be severed without any injury being done to the auditory nuclei in the medulla. The task of dividing the peduncle in this way was by no means as simple as might be expected, for it was found exceedingly difficult to divide the peduncle high enough to avoid injury to the auditory nuclei, and yet not so high as to include in the lesion parts of the cerebellum other than the fibres entering and leaving it by its inferior peduncle. Often when the appearances as seen with the naked eye seemed to indicate that this object had been attained subsequent microscopic examination showed that one or other of the auditory nuclei had been more or less injured. Then, again, the knife readily passed too far forward so as to sever fibres leaving the cerebellum by the superior peduncle; the higher the inferior peduncle was divided the more tendency was there for this complication to occur.

Attitude.—This was exceedingly characteristic, consisting in arching of the neck and trunk with the concavity to the side of the lesion so that the head and tail were approximated. There was little or no rotation of the head about the longitudinal horizontal axis of the body. The curving of the trunk becomes most obvious when the animal is disturbed, as when attempts are being made to induce it to stand. Under such circumstances, if the trunk be forcibly straightened it quickly returns to its former curved condition directly the force exerted to straighten it is taken off. Further, if for instance the left peduncle be divided the animal lies on its left side when at rest, and resists all attempts which may be made to place it to lie on its right side. If this resistance is forcibly overcome and the animal is placed to lie on its right side, it quickly rolls on to its left side directly the restraining force which is exerted to keep it on its right side is taken off. Sometimes so suddenly and vigorously does it roll over to the left side that it may, as it were, overstep the mark and roll over once or twice before coming to rest on its left side. The position of the limbs also calls for some comment. As the animal lies on its left side the usual condition in which they are found is one of flexion of the left extremities and extension of the right; but when it is disturbed all the extremities are usually extended. This last statement requires qualification however, for although true of what usually happens when the animal is first disturbed, it does not hold good throughout the examination, for it was found that the left hind limb, at any rate, was then held in a flexed condition when the animal was placed on its right side, or on its back.

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* The term "inferior cerebellar peduncle" is intended to include the restiform body and Edinger's direct sensory cerebellar tract.

All these conditions which have been described were most marked directly after the operation, and were characteristically present twenty-four hours later, when they can be most conveniently and satisfactorily examined, as presumably the animal may then be regarded as having recovered from the effects of the anæsthetic, and most of the shock consequent on the operation has passed off.

With regard to the spasm present in the limbs it is always exceedingly difficult, if not impossible in some cases, to distinguish between involuntary spasm of the muscles and voluntary spasm induced by the animal, owing no doubt to a sense of insecurity consequent on the lesion, and the uncertainty as to what is likely to take place during the examination.

When there was rotation it took place about the animal's longitudinal axis towards the side of the lesion, that is to say, in a left-sided lesion, the animal rotated like a right-handed screw entering an object; while in a right-sided lesion it rotated like a similar screw coming out of an object.

Disorders of Motility.—There is at first a complete inability to assume the standing position, and when attempts are made to place the animal to stand on its limbs, it fails entirely to support itself by them, and invariably falls over on to the side of the lesion. There appears to be an entire loss of all knowledge of how to use the limbs to support the body. When the left peduncle is divided the right limbs are at first usually kept extended, and the left more or less flexed; and even later when there is less of the spasmodic flexion of the left extremities, if an attempt is made to place the animal on all fours the left limbs appear to double up under it and it falls to the left side. The major part of these defects are unquestionably due to two factors, loss of muscular sense or the sense of position, and rigidity; but it is impossible to do otherwise than believe that another factor responsible for the inability on the part of the animal to stand is what is commonly known as motor paresis. The way in which the limbs on the side of the lesion appear to give way and double up under the animal when it is placed on all fours makes it difficult to avoid this conclusion. Further, as the animal recovers and first begins to stand it can only do so by supporting the side of the lesion against some steady object, such as on the walls of the room in which it is being examined. Then again, when it is possible for it to stand without such support it does so on a wide base, the limbs, both anterior and posterior, but more especially the latter, being widely separated from each other. If it attempts to shake itself, the limbs, more particularly the left, *i.e.*, on the side of the lesion, slide away from under the trunk, and the animal falls on to its left side. When it attempts to walk it does so in a sprawling manner, and as it further improves it becomes more and more possible, up to a certain point, to detect the uncertainty which exists with regard to the use of the limbs on the side of the lesion, and it is further possible to detect that when the animal falls, the posterior extremity on the side of the lesion is that which gives way first. Later, the animal becomes quite active, and walks and even runs about in an uncertain and ataxic manner, repeatedly falling on to its left side owing to the limbs on that side not being properly under the animal's control. The motor paresis does not affect all the limbs equally, but is most marked in the posterior extremity on the side of the lesion, less marked in the anterior extremity of the same side, and still less marked in the opposite posterior extremity, while the opposite anterior extremity appears to escape entirely. And, as has already been said, when power is being regained in the extremities the posterior extremity on the side of the lesion is that in which it is last restored.

Ocular Displacements.—Few facts in connection with the results of division of one inferior peduncle of the cerebellum are more definite than is the displacement of the globes which is to be seen after such a lesion. After the animal has recovered from the effects of the anæsthetic, both eyes are seen to be displaced downwards and to the opposite side from that on which the peduncle has been divided. If the left peduncle is divided, the displacement of the right eye is unquestionably greater than that of the left, especially as regards the degree of its displacement to the right; but in this connection, it has to be remembered that in the dog more sclerotic is visible on the inner than on the outer side of the cornea, and that, therefore, any displacement of the eye outward obtrudes itself on the observer more than does any displacement of the eye inward. Allowing for this source of fallacy, however, I still feel justified in stating that after division of one inferior peduncle the outward displacement of the opposite eye is greater than the inward displacement of the eye on the side of the lesion. Further, like all the other effects resulting from such a lesion, recovery takes place within a variable time, and in process of recovery it is invariably the eye on the side of the lesion which first returns to its normal position, the outward displacement of the opposite eye being obvious for a considerable time after the inward displacement of the eye on the side of the lesion has ceased to be detected.

The degree of displacement of the globes varies considerably in different animals; in some it is well marked, while in others it is slight; but in all it is present. So, too, the rate of improvement varies to a similar degree in different dogs, in some it passes off in a few days, while in others there is still some evidence of its existence, at any rate in the eye on the side opposite to that of the side of the lesion, two weeks after the operation. The time that the displacement persists largely depends on its degree in the first instance, those cases in which it is slight recovering more rapidly than those in which it is pronounced soon after the operation.

Apart from the actual displacement of the globes, and, indeed when this no longer exists, or is trivial, the animal appears to be unable to direct its eyes to the side of the lesion; at any rate, all attempts to induce it to do so, as a rule, fail, while it can be readily induced to direct its eyes to the opposite side when they are not very obviously displaced in this direction, or to turn them still further to this side, when the displacement, the result of the lesion, is considerable.

Further, even in those cases when there is only slight displacement of the globes after the operation, or where displacement has existed, but has recently been recovered from, the displacement can be brought about by placing the animal in some position in which, from its general behaviour, it is obvious that it is suffering from a sense of insecurity from loss of balance. When speaking of the attitude common to dogs in whom the inferior peduncle of the cerebellum has been divided on one side, for instance the left, I stated that such animals prefer to lie on the left side, and that they resist all attempts which may be made to place them on their right side; now when such attempts are made to place the animal to lie on its right side, this is one of the occasions when the abnormal displacement of the globes is intensified.

I have purposely avoided any mention of the position of the eyes in such animals after division of the inferior peduncle while they are still under the influence of the anæsthetic, because mention of this in my former paper on the cerebellum led to some misunderstanding, in that I was taken to mean that the displacement then observed was characteristic of the lesion, which was far from my intention. The only displacement of the eyes that can be regarded as truly characteristic of the lesion is that which exists after all influence of the anæsthetic has passed off. But there is another effect of the anæsthetic to which I wish to allude, and that is its influence with regard to the position assumed by the eyes after all displacement, the result of the operation, has passed off, and the animal is again placed under the anæsthetic influence of ether. In the stage which precedes that in which the eyes diverge—the stage, in fact, in which the eyes of normal dogs are displaced to one side or the other—the eyes of such dogs are displaced to the opposite side from that of the lesion, and this irrespective of the side to which they turned in the same stage of narcosis before the peduncle was divided. The effect of the anæsthetic in such animals, then, is to reproduce, at a certain stage of anæsthesia, the ocular displacement which at one time existed as a result of section of one inferior peduncle of the cerebellum.

Nystagmus.—Spontaneous nystagmus is rarely observed when the animal is at rest, but when disturbed and placed in some position in which it does not feel secure—as, for instance, when placed to lie on its right side when the left inferior peduncle has been divided—nystagmus is rarely absent during the first few days after the operation. As has been already said, any disturbing element responsible for increasing the animal's sense of insecurity increases the ocular displacement, and with this nystagmus usually results. The jerks are in the direction opposite to that of the ocular displacement; thus, if the eyes are displaced downwards and to the right, the nystagmoid jerks are upward and to the left. Of these two elements in the direction of the jerks, the upward usually is the more marked, but the combined effect adds a certain degree of rotation to the movements of the globes.

Sometimes the nystagmus occurs alone, but at other times it is accompanied by blepharospasm, constant blinking movements of the eyelids occurring simultaneously with the ocular jerks.

Reflexes.—Of all the phenomena which result from division of one inferior peduncle of the cerebellum, none are so difficult to be certain about as is the alteration in the state of the tendon reflexes. This difficulty is largely due to the amount of spasm of the muscles of the limbs, voluntary or otherwise. It is rarely possible to get the limbs sufficiently relaxed to be certain that the full effect of the response, as a result of the blow to the patella tendon, is being obtained. However, there seems little doubt that both knee-jerks are increased in activity as a result of the lesion; but the question does not end here, for it next becomes necessary to ascertain whether one knee-jerk is more increased than the other, and here comes the chief difficulty. Difficult as it is to get the animal to relax the muscles of one limb satisfactorily, it is still more difficult to obtain an equal degree of relaxation on the two sides at the same time, so that the most varying results are obtained; at one moment the one jerk appears to be the greater, at another moment the other. So that it is only by long, careful, and repeated observations that it becomes possible to venture on an opinion as to which knee-jerk is really the more active. Making all allowances for the difficulties which have to be overcome and fallacies to be guarded against, I am left with the impression that the knee-jerk on the side of the divided peduncle is greater than that on the opposite side; but I make the statement with great reserve, as, in the face of such difficulties, it is impossible to make a positive statement in this connection.

Disorders of Sensibility.—The extreme difficulty of testing sensation in animals, or rather of coming to definite conclusions with regard to the presence or absence of cutaneous sensibility, makes it important that we should only record those facts with regard to which there appears to be no question. In dogs I find it most difficult to be certain with regard to sensibility to tactile and thermal impressions, while there is very little difficulty in ascertaining accurately the condition as regards painful impressions. I therefore prefer to limit my observations at present to the state of sensibility to painful impressions. In testing this a metallic clip was used, of such strength as to be objected to by normal animals in a manner which left no room for doubt as to whether the animal, which was of course, blindfolded, was or was not aware of its presence on some portion of its cutaneous surface. Normal dogs tested in this way invariably objected when the clip was placed on any of the four extremities, and as far as could be ascertained the skin of the four extremities was sensitive to an equal degree to the stimulus.

Dogs in whom the inferior cerebellar peduncle was divided on one side gave evidence of most marked departure from this normal standard. For a variable time after the operation, usually about a week, the animal takes no notice of the clip when it is placed on any of the extremities, and that not only when the skin alone is pinched up, but when the clip is firmly pressed against the periosteum of some bone. The limb in which sensibility to painful impressions usually returns first is the anterior extremity of the side opposite to that of the lesion. There appear to be few exceptions to this rule in uncomplicated cases. The posterior extremity on the side of the lesion, on the other hand, is, as a rule, the last to recover; but it is less easy to speak definitely with regard to the order of restoration of sensibility to painful impressions in the other extremities; sometimes the posterior extremity of the opposite side, at other times the anterior extremity on the side of the lesion, is the second to recover. But in spite of this fact of the posterior extremity on the side of the lesion being last to recover when sensibility to painful impressions returns in all the extremities, the animal may appear to be more sensitive to painful impressions on the posterior extremity of the side of the lesion than on the opposite side.

When sensibility to painful impressions is first returning the animal only takes notice of the clip when it is pressed firmly against the periosteum of some bone; but, as further improvement occurs, the pinching up of the skin alone is objected to, and in the end they respond to the stimulus in the same way that normal dogs do. There is always return of sensibility to painful impressions before the improvement in motility is sufficient to allow the animal to stand or walk.

6. The Effects of Partial Section of the Lateral Region of the Medulla on one side interrupting the Lateral Medullary and Direct Cerebellar Tracts (Control).

The section of the medulla was made transversely and in such a way as to avoid injury to the posterior columns and their nuclei on the one hand, and the pyramid on the other. In order to accomplish this successfully a narrow-bladed delicate knife was inserted just external to the posterior columns, its point was brought out just externally or dorsally to the inferior olive, and the knife was then made to cut its way out of the portion of the medulla thus transfixed.

Attitude.—The attitude assumed by such an animal, after it had recovered from the effects of the anæsthetic, resembled closely that of a dog whose inferior cerebellar peduncle had been divided close to the point where it enters the organ. The neck and trunk were curved with the concavity of the curve to the side of the lesion, but the curving of the neck was much more pronounced than was that of the trunk. There was, however, no twisting of the head by rotation of the neck on its longitudinal axis so as to turn either side of the animal's face upward. If the neck and trunk were forcibly straightened they quickly returned to their abnormal position when the restraining force was taken off, and it was easy to satisfy one's self that the curving of the neck and trunk with the concavity of the curve to the side of the lesion was due to an actual spasm of the muscles on that side of the body.

There was inability to stand or walk, and the animal evidently felt more secure when placed to lie on the side of its body corresponding to the lesion than when placed to lie on the side opposite to the lesion. The latter procedure resulted in only a limited portion of the animal's body remaining in actual contact with the ground, for the curving of the neck and trunk was exaggerated under these circumstances, and thus the head and posterior quarters of the animal became approximated to each other and both were raised off the ground. When there was rotation of the animal, which did not always occur, it did so round its longitudinal axis like a right-handed screw entering an object when the lesion was on the left side, a direction which, according to my previous descriptions I have regarded as rotation to the side of the lesion.

Disorders of Motility.—These closely resembled those which resulted on section of the inferior peduncle of one side at its point of entrance into the cerebellum.

The animal was at first unable to stand, and in all attempts to do so the posterior extremities remained flexed under it, but it raised the fore part of its body by means of its anterior extremities. This position was, however, only momentarily maintained, as the anterior extremity on the side of the lesion quickly doubled up under the animal and as a result it invariably fell over on to that side. As the animals recovered the posterior extremity on the side of the lesion was the last in which power was restored, and there were many ways in which this was shown. Such an animal after apparent recovery will sometimes stand on three legs and scratch its head with the posterior extremity on the side of the lesion, while it will make no such attempt to stand on three legs while using the opposite posterior extremity to scratch its head with. Indeed, I have seen such animals, after scratching with the posterior extremity on the side of the lesion while standing on the other three extremities, deliberately lie down and then scratch the other side of their heads with the opposite posterior extremity.

Then again, if the animal happens to be a male, long after it appears to have regained motor power completely, it makes no attempt to pass urine in the way common to most male dogs, that is by raising one posterior extremity; on the contrary such dogs invariably urinate like puppies, simply lowering the posterior part of the trunk by flexing the posterior extremities.

These supplementary remarks with regard to evidences of defective power more especially in the posterior extremity on the side of the lesion, though made here, apply equally to those animals in which the inferior cerebellar peduncle has been divided on one side close to the cerebellum.

Ocular Displacements.—The positions of the globes depended largely on the exact extent of the lesion. If the lesion was extended far enough forward so as to include the whole of the direct cerebellar tract, then the position of the globes was similar to that which resulted when the inferior peduncle was divided close to the cerebellum, that is, both eyes are turned downwards and away from the side of the lesion, this being well marked in the opposite eye and only slightly evident in the eye on the side of the lesion. In those cases on the other hand in which the lesion was limited, involving only the lateral region of the medulla in close proximity to the posterior columns without dividing the direct cerebellar tract, the eyes were displaced to the side of the lesion instead of to the opposite side, and this displacement was more pronounced in the globe on the side of the lesion than in the opposite one. There was, however, the same element of downward rotation of the globes in both instances.

The ocular displacements could be intensified by putting the animal in some position in which it evidently felt insecure, as for instance by placing it to lie on the side of the body opposite to that of the lesion.

As in the displacements of the globes which result from lesions of the cerebellum or its inferior peduncle, so in the case of section of the lateral region of the medulla the ocular displacement was only temporary and was gradually recovered from, so that, as a rule, within a week of the time of the operation the eyes recovered their normal positions.

Nystagmus.—No nystagmus was detected when the animal was at rest, and even when the animal was placed in some position which appeared to increase its feeling of insecurity, and which resulted in an intensification of the ocular displacement, no nystagmus was observed.

Reflexes.—The same difficulty which was met with in testing the knee-jerks after division of the inferior cerebellar peduncle was encountered in the case of these experiments also. The posterior extremities were so constantly held in a state of flexor spasm when an attempt was being made to elicit the knee-jerks, that it was really quite impossible to arrive at any positive opinion as to the full degree of their increased activity, and as to which of the jerks was the more increased; but as far as could be judged, the left jerk appeared to be slightly the more active of the two. In some animals there could be little question as to the left being the greater, but in others it was exceedingly difficult to be certain.

Disorders of Sensibility.—The day after the operation such an animal took no notice of the painful clip when this instrument was placed on any of the extremities, and this condition of analgesia persisted for some time after the operation, finally clearing up in the same order, as regards the four extremities, as has been detailed in connection with section of the inferior cerebellar peduncle. The opposite anterior extremity is that on which the animal first begins to take notice of the clip, and the posterior extremity on the side of the lesion is the last in which there is evidence of return of sensibility to painful impressions. As in the case of the inferior peduncle, so here there was a good deal of variability as regards which of the other two extremities first recovered sensibility.

7. The Effects of Transverse Section of the Posterior Columns on One Side a Few Millimetres Above the Calamus Scriptorius (Control).

Dogs on whom this operation was performed presented a very different picture to those in whom the inferior peduncle was divided close to the cerebellum, or in whom the lateral tracts of the medulla were severed. The lesion was effected by means of a delicate narrow-bladed knife, which was made to enter the middle line of the medulla posteriorly, about two or three millimetres above the calamus scriptorius, and to pass transversely outwards, so as to divide both the funiculus gracilis and funiculus cuneatus with their respective nuclei.

Attitude.—The animals were, as a rule, able to stand and walk a few hours after they had recovered from the effects of the anæsthetic. The trunk was curved, with the concavity to the side of the lesion, as in the case of division of the inferior cerebellar peduncle. The neck was also curved, with its concavity in the same direction, and the head was twisted on the trunk, so that one or other side of the face was turned to a varying degree upward, while the other side of the face was, of course, turned downward; but the same side of the face was not always turned upward, for while in most cases that on the side of the lesion was so turned, in other cases it was the opposite side of the face which was turned upward. When the latter was the case, it was not so pronounced, however, as when the side of the face corresponding to the side of the lesion was that which was turned upward.

Disorders of Motility.—In standing and in walking the posterior part of the trunk was at a lower level than the anterior, owing to the posterior extremities being kept in a semiflexed condition. This gave the animal a curious appearance during progression, which was rendered still more striking by the fact that in moving forward the dog did so sideways, like a crab, so that the side of the lesion was constantly kept facing towards the direction in which the animal was walking.

These defects were gradually recovered from, the twisting of the head on the neck and the arching of the trunk being the first to pass off. The position of the posterior extremities and the inclination to keep the side of the lesion forward during progression were more lasting symptoms, and did not entirely pass off in some cases until a fortnight had elapsed after the operation.

Ocular Displacements.—The reverse of what obtains in the case of a lesion of the inferior cerebellar peduncle was met with in these cases where the posterior columns on one side were divided, for the eyes were displaced to the side of the lesion instead of to the opposite side. The two lesions have one thing in common in this connection however, in that in both cases the eyes were directed downwards. As in the case of the peduncle, so here, the displacement was not equally marked on the two sides, but, whereas in the former case it was the opposite eye that was most displaced, in the case of the posterior columns it was the eye on the side of the lesion which was most obviously displaced.

When such animals were induced to look to the side opposite to that of the lesion, the opposite eye moved better and farther in that direction than did the eye on the side of the lesion.

The ocular displacement was recovered from in the course of a week, the opposite eye recovering before that on the side of the lesion.

Even after they had recovered, however, and could be moved well to either side, traces of the former defect could be detected when the animal was lifted, placed on its back or side, or otherwise suddenly disturbed or agitated.

So too, if placed under the anæsthetic influence of ether after the eyes had returned to their normal positions, the displacement downwards and to the side of the lesion was reproduced during the stage of narcosis which immediately preceded that in which the eyes diverged.

Nystagmus.—The occurrence of nystagmus was certainly not the rule; there was, however, one case in which it was present, but here the lesion was not limited to the posterior columns, but extended more deeply so as to injure the lateral region of the medulla. In the case in question there was well-marked lateral nystagmus, and the eyes were displaced to the side of the lesion as in other cases of transverse section of the posterior columns on one side, and not to the opposite side as in the cases in which all the lateral tracts of the medulla were divided and the posterior columns and their nuclei were left intact.

Reflexes.—There appeared to be some increased activity of the knee-jerks, though not to the same extent as after division by the inferior peduncle of the cerebellum high up or section of the lateral tracts of the medulla. It was exceedingly difficult to be certain of any real inequality of the knee-jerks owing to the fact that there always appeared to be a certain amount of flexor spasm of the posterior extremity on the side of the lesion, while the muscles of the opposite posterior extremity were much more relaxed during the examination. How much of the flexor spasm in the posterior extremity on the side of the lesion was voluntary and how much involuntary it was difficult to estimate. When the muscles of the limb on the side of the lesion were relaxed, the knee-jerk on that side appeared to be more active than that on the opposite side; but the difficulties which attended the examination made it impossible to speak with any degree of certainty on a point where comparatively slight differences were being dealt with.

Disorders of Sensibility.—As in the case of the experiments on the inferior cerebellar peduncle so in these experiments, I confined my attention entirely to the presence or absence of the power of conduction of painful impressions. A few hours after the operation, when the animals had so far recovered from the immediate effects of the operation as to be able to walk a little, though imperfectly, they took no notice of the clip when this was placed on any of the extremities. This defective conduction of painful impressions was still evident on the following day, but afterwards began to show signs of improvement. The order in which the limbs recovered in this respect was quite constant, but the tendency appeared to be for the anterior extremities to recover before the posterior, and for the limbs of the opposite side to recover before those on the side of the lesion.

8. COMPARISON OF THE ELECTRICAL EXCITABILITY OF THE TWO CEREBRAL HEMISPHERES.

(A.) *One Inferior Cerebellar Peduncle divided.*

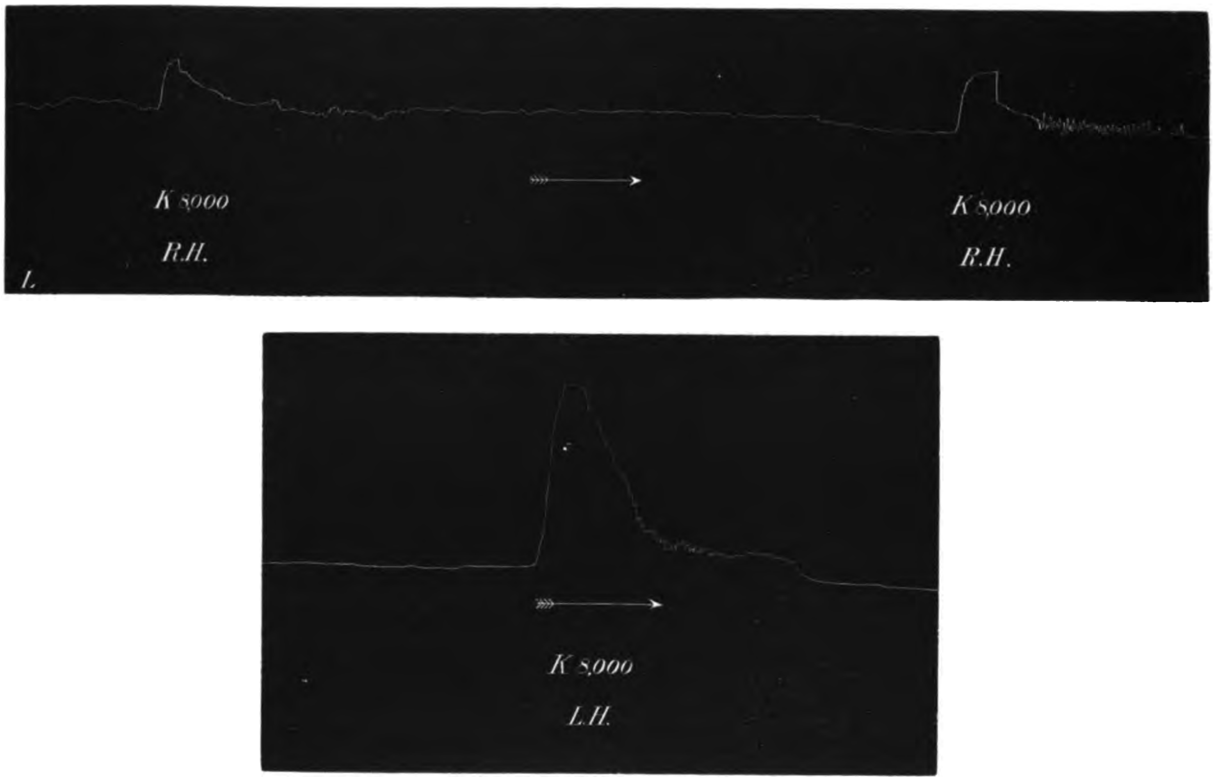
The greatest possible care was taken not to injure the cortex on either side when the cerebral hemispheres were being exposed, and to avoid any pressure on the cortex. The two hemispheres were placed as far as possible in exactly the same conditions, and the cortex of each was kept warm and irrigated from time to time with warm normal salt solution.

The extensor muscles of the anterior extremities were exposed, separated from their attachments to the lower two-thirds of the bones of the forearms, and while their proximal attachments were left intact the distal ends of their tendons were divided and connected with spring myographs, whose springs were as nearly as possible equal, and records of the muscular contractions were taken in the way that has been described earlier in this paper.

The time at which the inferior cerebellar peduncle on one side was divided varied; sometimes this was the first part of the operation, at other times it followed the exposure of the extensor muscles of the forearm, and at other times it followed the exposure of the cortex of the cerebral hemispheres, which part of the operation was always preceded by exposure of the extensor muscles. At whatever period in the course of the operation the peduncle was actually divided, the exposure of the cerebellum and preparation for subsequent division of the peduncle was always the first step undertaken.

Testing of the electrical excitability of the cortex always followed immediately on the completion of the various preliminaries that have just been detailed. The fore-limb area of each hemisphere was carefully explored in order to find, if possible, a focus in each excitation of which most readily resulted in a response from the extensor muscles of the fore limbs. At other times, a point as nearly as possible in the same position on the two sides was chosen, and the excitability of the cortex at this point on each side carefully tested. The results obtained by the one method of procedure were thus checked by those obtained by the other method.

Fig. 1.



Records of response obtained when the cortex of the cerebral hemispheres was excited with a current of 8000 on KRONECKER'S scale, soon after section of the left inferior peduncle of the cerebellum.

R = right anterior extremity. L = left anterior extremity.

R.H. = right cerebral hemisphere. L.H. = left cerebral hemisphere.

The results varied according to the extent of the lesion of the inferior peduncle, that is to say the more completely was the peduncle divided, the greater was the difference of excitability of the cortex noted on the two sides. This only held good as long as the lesion was strictly limited to the inferior peduncle, however, for although this might be completely divided, the effect would be considerably modified if any considerable portion of the fibres of the superior cerebellar peduncle were also included in the lesion.

So long as the lesion was limited to the fibres of the inferior peduncle on one side, the greater the completeness of division of this structure the less excitable was the opposite cerebral hemisphere as compared with its fellow, and as tested by the response obtained from the extensor muscles of the fore-arm of the anterior extremity of the animal. So that if the left inferior peduncle was the one divided, the response from the extensor muscles of the left fore-limb on excitation of the right cerebral hemisphere, was less than the response obtained from the muscles of the right fore-limb on excitation of the left cerebral hemisphere. Thus in an experiment in which the left inferior peduncle was divided, an induced current with the secondary coil at 400 on **Kronecker's** scale, and with the inductorium supplied by a single bichromate cell, failed to elicit any response in the extensor muscles of the left fore-limb when the right cerebral hemisphere was excited, while the same current when applied to the left cerebral hemisphere evoked well-marked contraction in the extensor muscles of the right fore-limb. Then again in an animal in which the same lesion had been produced, an induced current with the secondary coil at 8000 on **Kronecker's** scale,

Fig 2.

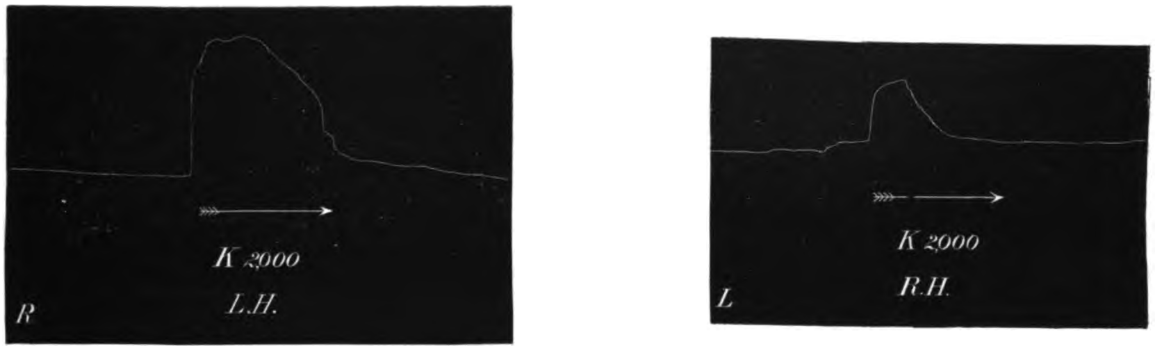
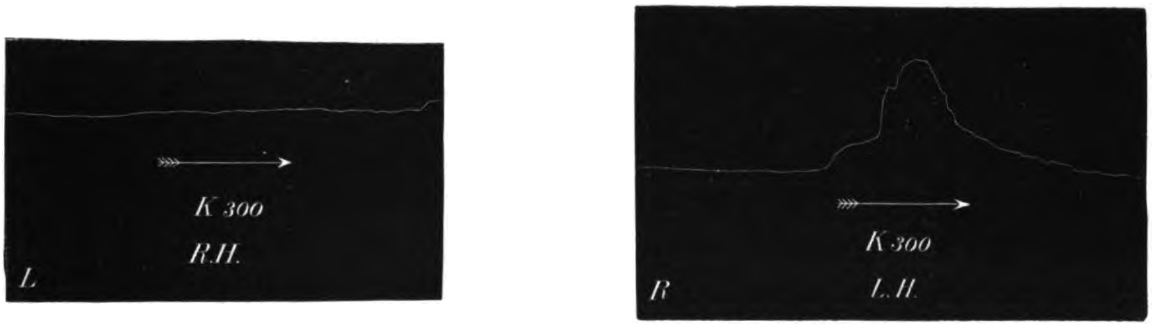


Fig. 3.



Records of response obtained from the extensor muscles of the fore-arms on stimulation of the cortex of the cerebral hemisphere with a current of 2000 and one of 300 on Kronecker's scale, in an animal soon after section of the left inferior cerebellar peduncle.

R. = right anterior extremity. **L. = left anterior extremity.**
R.H. = right cerebral hemisphere. **L.H. = left cerebral hemisphere.**

gave a greater response in the extensor muscles of the right anterior extremity on excitation of the left cerebral hemisphere than resulted in the muscles of the left anterior extremity when the right hemisphere was excited (see fig. 1). The same result was obtained with the secondary coil at 4000 and at 2000 (see fig. 2), while with the secondary coil at 300 on the same scale, there was no response from the extensor muscles of the left fore-limb when the right hemisphere was excited, while the muscles of the right anterior extremity responded distinctly when the left cerebral hemisphere was stimulated (see fig. 3).

(B.) *Partial Hemisection of the Medulla.*

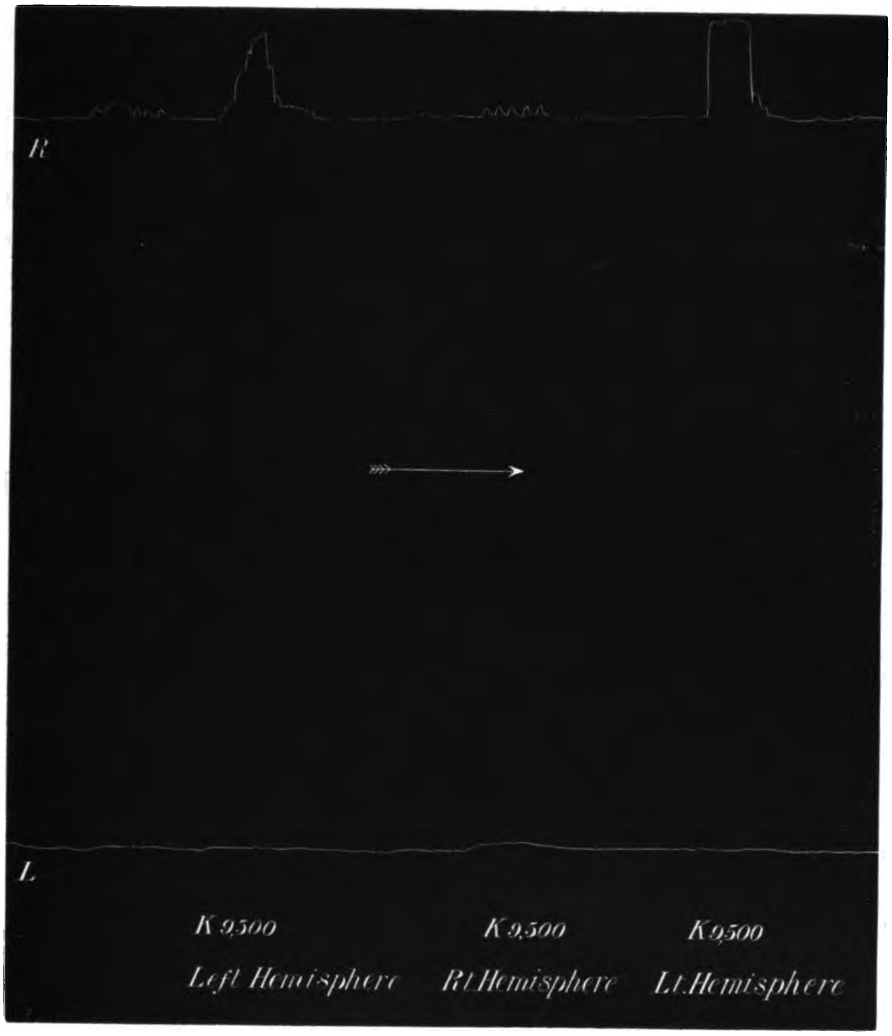
In one series of experiments instead of dividing the inferior peduncle close to the cerebellum, partial hemisection of the medulla on one side about 3 or 4 millims. above the calamus scriptorius was performed. In this operation the knife was passed from the middle line posteriorly through the whole thickness of the medulla from behind forward, but slightly obliquely so as to just avoid injury to the pyramid, it was then made to cut its way out of the medulla transversely. In some cases the pyramid appeared to escape injury completely, while in others a variable number of the outer fibres of this structure were included in the lesion.

When the lesion was on the left side and the pyramid escaped, or the injury to it was only trivial, induced currents of sufficient intensity to evoke a response from the extensor muscles of the right fore-limb when the left cerebral hemisphere was excited, failed to elicit any response in the muscles of the left fore-limb when the right hemisphere was stimulated.

But not only was a difference in the excitability of the two hemispheres observed when stimuli of moderate intensity were employed, but also in some cases when stimuli of sufficient intensity to evoke general epilepsy were used. Under these circumstances a stimulus applied to the left cerebral hemisphere, when the left inferior peduncle was divided, evoked general epileptic spasms in which all the muscles of the body appeared to be involved except those of the left anterior extremity, the exposed extensor muscles of whose fore-arm remained quite passive throughout the otherwise general convulsions. Although the muscles of both posterior extremities were in spasm under these circumstances, it was easy to see that those of the left posterior extremity were contracting less vigorously than those of the right posterior extremity.

Striking as was this result, in which the muscles of the fore-limb on the side of the lesion remained passive during otherwise general epileptic convulsions induced by excitation of the cortex of the cerebral hemisphere concerned chiefly with the production of movement on the opposite side of the body, it was still more remarkable to find that even a current of sufficient intensity to evoke general epileptic convulsions when applied to the opposite cerebral hemisphere, that is, that concerned chiefly with the movements on the side of the body on which the hemisection of the medullar has been performed, failed to elicit contraction in the extensor muscles of the anterior extremity on the side of the lesion.

Fig. 4.



Records of response obtained from the extensor muscles of the fore-limbs, on stimulation of the cortex of the cerebral hemispheres with a current of 9,500 on KRONECKER'S scale, in an animal soon after lateral section of the medulla on the left side.

R = right anterior extremity; L = left anterior extremity.

Fig. 4 is a record of the contractions of the extensor muscles of the right anterior extremity of an animal in whom partial hemisection of the medulla was performed on the left side, and shows that, with a current of 9,500 on KRONECKER'S scale, applied to the left hemisphere, well marked contractions resulted in the muscles of the right anterior extremity, while the muscles of the left anterior extremity recorded no such contractions when the same strength of current was applied to the right cerebral hemisphere.

9. CONVULSIONS INDUCED BY INTRAVENOUS INJECTION OF ABSINTHE.

(A.) *One Inferior Cerebellar Peduncle divided.*

(1.) **Immediate Effect.**
(2.) **Remote Effect.**

In my former paper it was shown that absinthe convulsions induced in normal animals resulted in muscular contractions which had the same characters on the two sides of the body, so that tracings taken from the extensor muscles of the fore-limb of the dog showed clonus, followed by tonus ending in clonus. In animals in whom the inferior peduncle of the cerebellum was divided on one side, a striking alteration was observed, the precise nature of which depended on whether the convulsions were induced immediately after section of the peduncle or at some remote period.

Immediate Effect.

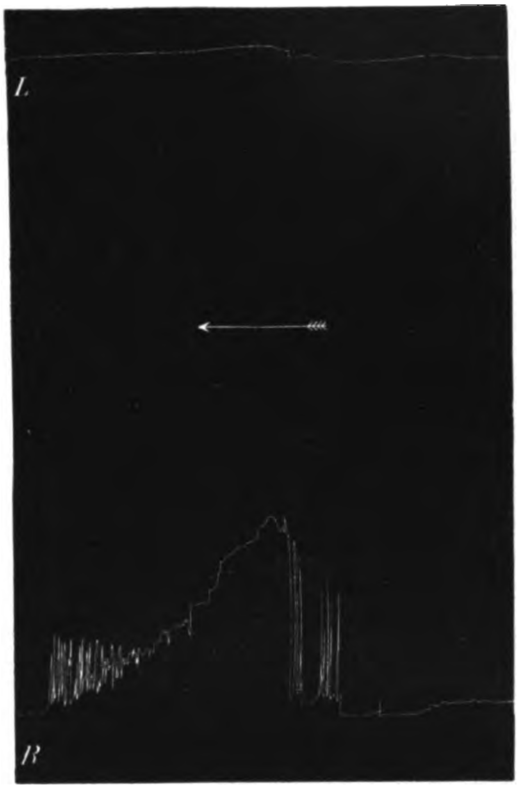
(1.) The immediate effect was much the more striking of the two, and consisted in an entire absence of convulsions in the muscles of the anterior extremity on the side of the lesion. Not only did the writing-point of the spring myograph not record any contractions of the muscles, but by direct observation it was easy to satisfy myself that the muscles of this extremity remained inactive, while all the other muscles of the animal seemed to be actively contracting. When tracings were taken of the convulsions in the posterior extremities, they showed no such remarkable difference on the two sides; but the convulsions in the muscles of the limb on the side of the lesion were less powerful than were those in the opposite posterior extremity.

Fig. 5 shows this effect very clearly, the records being taken from an animal in whom the left inferior cerebellar peduncle was divided, and absinthe convulsions were induced at the time of the operation, that is soon after the section of the peduncle. Here it may be seen that while the extensor muscles of the right anterior extremity recorded well-marked convulsions, there is absolutely no sign of the record of a convulsion in the extensor muscles of the left anterior extremity, the writing-point of the spring myograph with which they were connected recording a more or less straight line throughout the period, during which the writing-point of the other myograph was recording the active muscular contractions of the extensor muscles of the right anterior extremity.

In all cases the muscles first connected with one myograph were afterwards connected with the other, and further epileptic convulsions induced in order to exclude the possibility of one myograph being more easily acted on than the other, and thus accounting for the remarkable difference observed in the records from the two fore-limbs. This precaution was superfluous, however, for as has already been said, direct observation of the exposed extensor muscles, during the epileptic convulsions, alone served to place beyond doubt the fact that the muscles of the right extremity were in vigorous contraction, while those of the left extremity remained absolutely passive.

Not only was this effect observed in the first or first few convulsions evoked, but provided the division of the inferior peduncle had been fairly complete, and the lesion had not involved, to any extent, the fibres of the superior peduncle, it could be repeated time after time in a series of convulsions of considerable number.

Fig. 5.



Result of convulsions induced by absinthe in an animal soon after the left inferior peduncle of the cerebellum was divided. Tracing obtained from extensor muscles of fore-arm.
R = right. L = left.

(2.) *Remote Effect.*

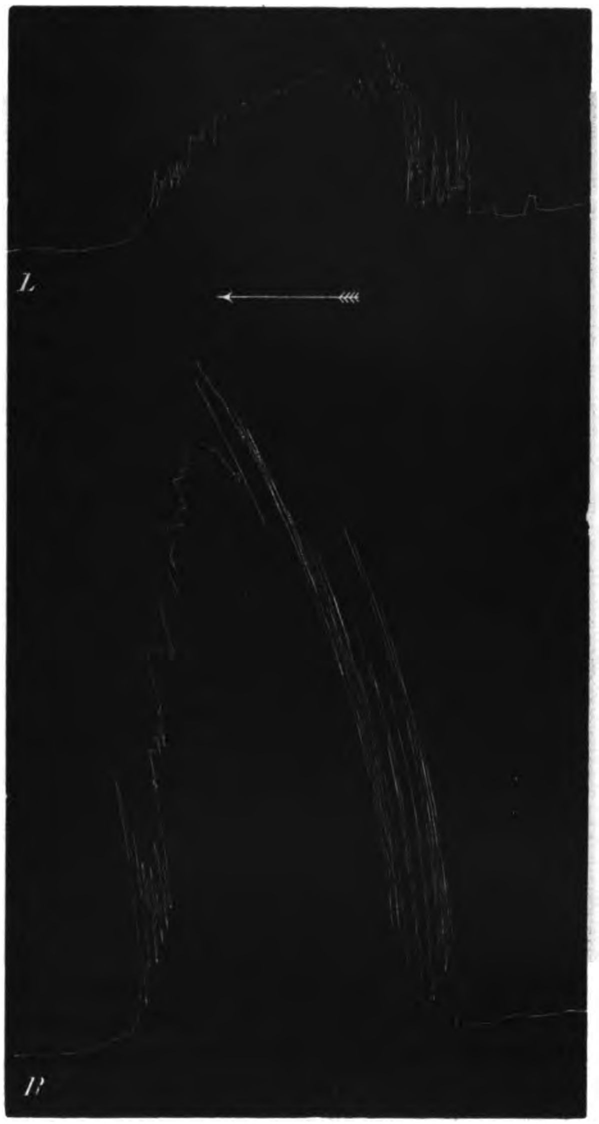
If, instead of inducing convulsions in the animal a short time after the inferior peduncle on one side was divided, it was allowed to live for three weeks or so, and the convulsions evoked in it by intravenous injection of absinthe, the state of things which resulted differed very markedly from that met with when the convulsions were evoked immediately after the section of the peduncle. There was no longer an absence of convulsions in the extensor muscles of the anterior extremity of the side of the lesion, but, nevertheless, the character of the convulsions in the two anterior extremities differed in important respects, as shown by tracings obtained by means of the spring myographs. Such tracings showed a much greater degree of tonic convulsion in the muscles on the side of the lesion as compared to those of the anterior extremity of the opposite side, where there was much less tonus, its place being taken by clonic contractions. Like the immediate effect, these differences could be made out without the aid of the tracings, by direct observation of the exposed extensor muscles of the fore-limbs on the two sides. In addition to this difference as regards tonus and clonus on the two sides, the contractions of the muscles of the left anterior extremity were less powerful than were those of the right anterior extremity. Indeed, in cases in which practically no other differences in the characters of the convulsions could be detected on the two sides, this difference in the amount or power of contraction could be well seen. Fig. 6 is the record of the contractions of the extensor muscles of the two anterior extremities of a dog whose inferior peduncle was divided on the left side about three weeks before the records were obtained. General epileptic convulsions were induced by absinthe, and, as may be seen from the figure, while there was very little difference as regards clonus and tonus on the two sides, the amount of power of contraction on the right side was much in excess of that on the left. In such experiments, as in the case of the former ones, the myographs were always subsequently reversed, the muscles first connected with one myograph being afterwards connected with the other, to exclude the possibility of the differences in the character of the recorded contractions being due to any differences in the springs of the myographs. In all cases the tension of the strings connecting the muscles with the myographs was kept as nearly as possible equal on the two sides.

Such were what may, for convenience of description, be called the pure immediate and remote effects of section of one inferior peduncle of the cerebellum in modifying the convulsions induced by absinthe. These results were, however, only obtained when the lesion was fairly limited to the inferior peduncle and yet divided the greater portion of this structure. The fewer the fibres divided in the peduncle the less likely were these effects to be observed, and the more other parts of the cerebellum, especially the superior peduncle on the same side, were involved in the lesion, the more likelihood was there that these phenomena would not result. Indeed in those cases where the extension of the lesion to the superior peduncle was at all serious, both the immediate and remote effects observed during absinthe convulsions showed a greater degree of contraction in the extensor muscles in the fore-limb on the side of the lesion than in that of the opposite side, the reverse of what was obtained in lesions limited to the inferior peduncle on one side.

(B.) *Partial Hemisection of the Medulla.*

Hemisection of the medulla so performed as to divide all the structures on one side with the exception of the pyramid led to modifications in the results of the absinthe convulsions as remarkable, and indeed identical with those observed after section of one inferior peduncle of the cerebellum. There was the same absence of contraction of the extensor muscles of the fore-limb on the side of the lesion during otherwise general convulsions in which the extensor muscles of the opposite anterior extremity took an active part. As in the case of the inferior peduncle, so here, not only did the records obtained with the myograph indicate this difference, but actual observation of the exposed muscles left no room for doubt that the records gave a

Fig. 6.

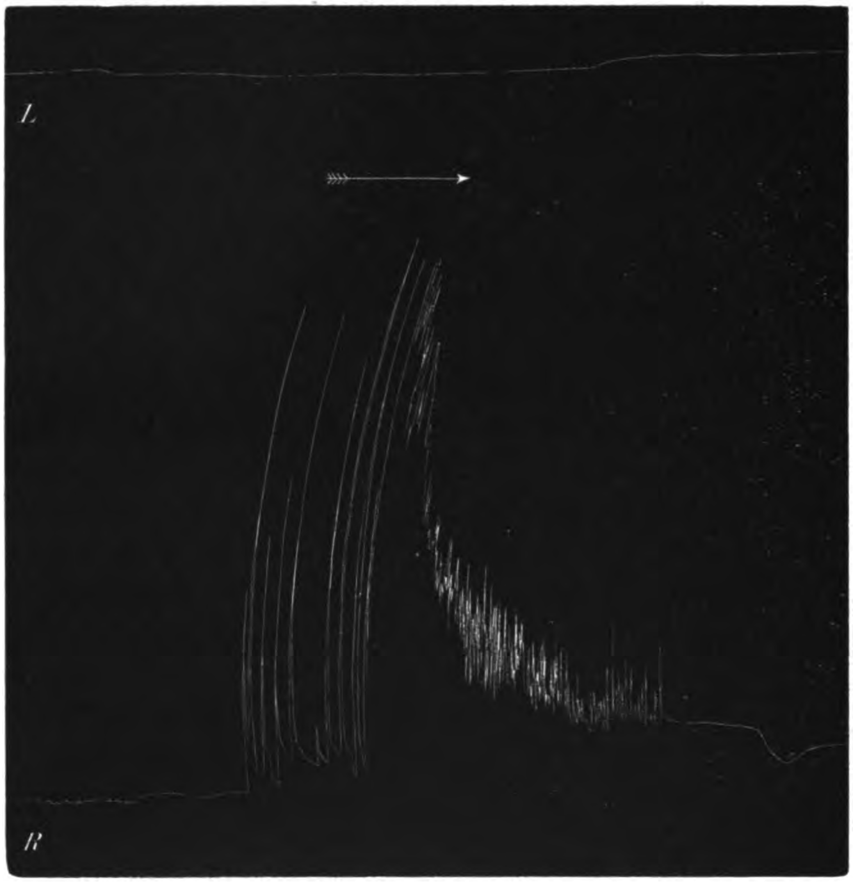


Result of Convulsions induced by absinthe in an animal three weeks after the left inferior peduncle of the Cerebellum was divided.

R—right anterior extremity. L—left anterior extremity.

true account of what was actually taking place in the muscles of the limbs, those of the anterior extremity on the side of the lesion being quite passive and free from spasm of any kind. The well-marked muscular contractions of the extensor muscles of the right anterior extremity are well shown in fig. 7, which is a tracing taken from an animal in whom partial hemisection had been performed on the left side of the medulla a short time before the convulsions were evoked by absinthe, and which shows equally clearly how the writing-point of the myograph connected with the extensor muscles of the left anterior extremity preserved a comparatively straight line during the time that these vigorous muscular contractions were going on in the opposite fore-limb.

Fig. 7.



Result of convulsions induced by absinthe in an animal in whom partial hemisection of the medulla was performed a short time before the tracing was taken.
R = right anterior extremity. L = left anterior extremity.

The resemblance between the effects of partial hemisection of the medulla and division of one inferior peduncle of the cerebellum, were further borne out by the way in which the absinthe convulsions affected the muscles of the posterior extremities, for the muscles of both these limbs were in active contractions during the convulsions, but the contractions of the muscles on the side of the lesion were less powerful than were those on the opposite side.

In some instances a considerable number of the fibres of the pyramid were accidentally divided with the other structures on one side of the medulla, in which case the extensor muscles of neither anterior extremity contracted in some instances, and while the muscles of both posterior extremities contracted, those of the opposite limb did so less powerfully than did those of the limb on the same side as the lesion.

(c.) *Transverse Section of the Posterior Columns and their Nuclei on one side.*

The lesion in these cases was made in such a way as to include the *funiculus gracilis* and *funiculus cuneatus* with their nuclei, without extending so far forward as to divide the lateral medullary and direct cerebellar tracts.

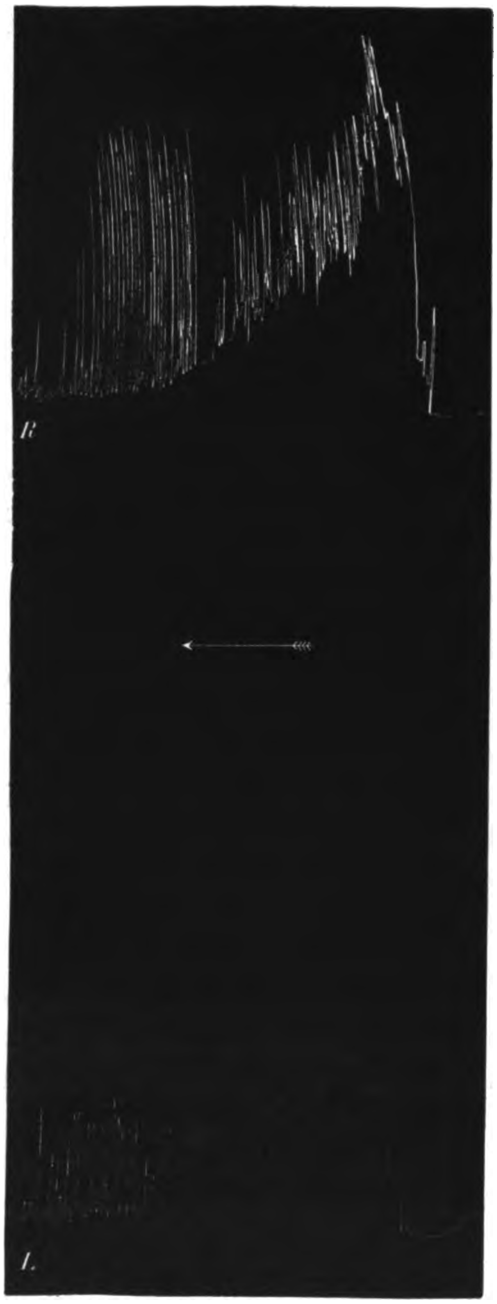
Absinthe convulsions induced in animals in whom this operation had been performed, showed a difference in the characters of the curves representing the contractions of the extensor muscles of the two anterior extremities, but both the immediate and remote effects resembled the remote effect produced by division of the inferior cerebellar peduncle on one side rather than the marked effect so characteristically seen when convulsions are evoked in an animal immediately after the inferior peduncle has been divided on one side. The extensor muscles of both fore-limbs contracted during the absinthe convulsions, but the muscles of the limb on the side of the lesion contracted less powerfully than did those of the opposite side, and there was more tonus in the muscles on the side of the lesion, there being no clonic contractions in these muscles in some instances. Fig. 8 shows the early effect in an animal whose posterior columns and their nuclei were divided on the left side, and absinthe convulsions induced two weeks afterwards. The tracing shows clearly how the muscular contractions of the left anterior extremity were not only smaller in amount than those on the right side, but also largely tonic in character, as opposed to the large amount of clonus shown in the tracing of the muscles on the right side.

Fig. 9 represents the same condition of things in an animal in whom absinthe convulsions were induced about two weeks after the posterior columns and their nuclei were divided on the left side, the record being one taken towards the end of a long series of convulsions of which fig. 8 is a representation of one of the earlier ones. This figure shows how much the amount of contraction becomes diminished on the left side, and how all clonus is absent from the convulsions on that side.

10. DISCUSSION OF RESULTS.—CONCLUSIONS.

The phenomena which result from section of one inferior peduncle of the cerebellum considered in conjunction with former results which I obtained from ablation of one lateral half of the cerebellum, and others from intracranial section of the auditory nerve, appear to me to afford us valuable information with regard to many of the functions of the cerebellum; but they cannot be said to settle definitely the all-important question as to whether the cerebellum exercises a direct downward

Fig. 8.

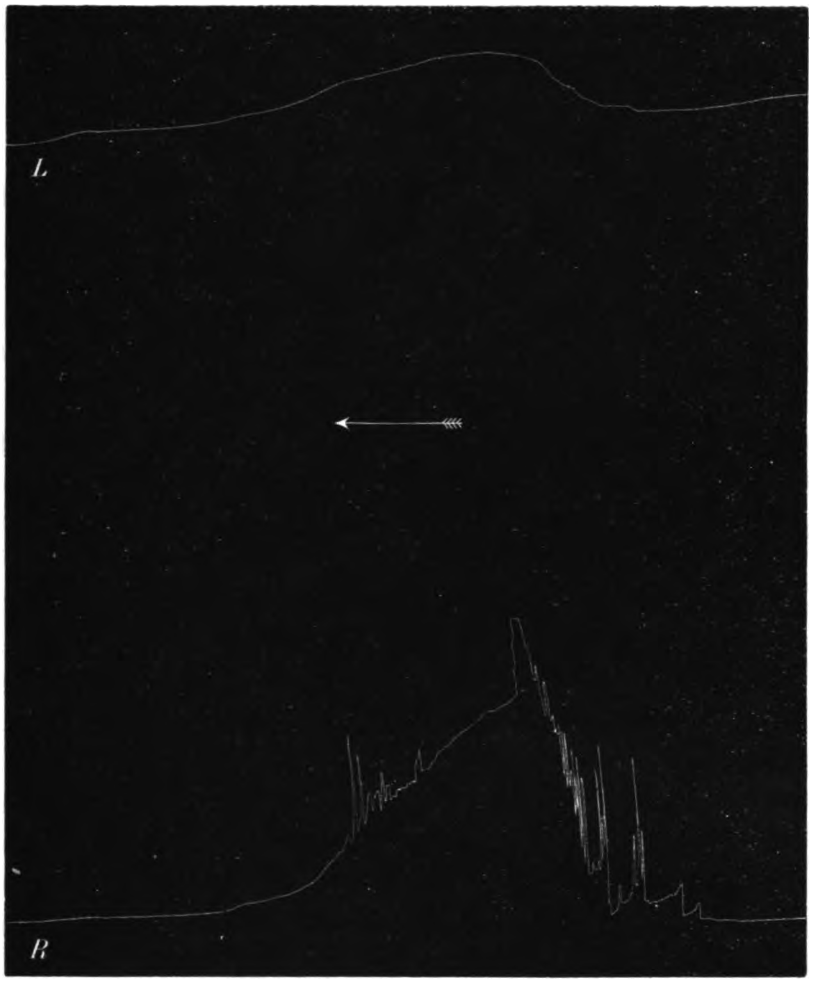


Result of convulsions induced by absinthe in an animal two weeks after division of the left posterior columns and their nuclei in the medulla. The tracings represent one of the earliest of a series of convulsions.

R = right anterior extremity. L = left anterior extremity.

influence on the spinal centres or not. Many of the results obtained by division of one inferior peduncle of the cerebellum suggest the possibility of such a downward influence, as was also suggested by the results of ablation of one lateral half of the organ; but none of them can be claimed as absolute and incontrovertible evidence of the existence of such an influence exercised by the cerebellum on the spinal centres, and through them on the muscles. All the effects which point to this possibility can as readily be explained by supposing that they are the result of the cutting off of afferent impulses from the periphery towards the cerebellum as a centre, as will become evident if we briefly review the effects obtained.

Fig. 9.



Result obtained towards the end of a long series of convulsions induced by absinthe in an animal two weeks after division of the left posterior columns and their nuclei in the medulla.
R = right anterior extremity. L = left anterior extremity.

That the disorders of co-ordination are the result of the interruption of afferent impulses passing from the periphery to the cerebellum does not admit of much doubt. It is interesting to note that whereas an animal deprived of, for instance, the left half of its cerebellum rotates like a right-handed screw coming out of an object (what I have described as rotation away from the side of the lesion), one in which the left inferior peduncle of the cerebellum is divided rotates like a right-handed screw entering an object (what I have described as rotation to the side of the lesion). This point is of further interest when we remember that intracranial section of the auditory nerve was responsible for rotation in exactly the same direction as that in which the animal rotates when one of the inferior peduncles of the cerebellum is divided; that is to say with a left-sided lesion in both cases the animal rotates like a right-handed screw entering an object.

That the bulk of the afferent impulses, whose interruption are responsible for this phenomenon, reach the cerebellum by way of the auditory nerve and the inferior cerebellar peduncle is evident from the above considerations, but that all of the impulses do not reach the peduncle from the auditory nerve is made clear by the fact that lateral section of the medulla below the auditory nerve and its nucleus sometimes results in similar rotation of the animal about its longitudinal axis. And although such rotation does not always result from this lesion, yet the other indications of disturbance of equilibration are the same when these tracts are interrupted far back in the medulla as when the inferior peduncle is itself divided close to the cerebellum.

At first sight the disorders of motility would appear to lend strong support to the view that the cerebellum has a downward action on the muscles of the limbs through the spinal centres, but that such a conclusion is open to serious question is evident from a consideration of the results obtained by CLAUDE BERNARD* in frogs and puppies, and by MOTT and SHERRINGTON† in monkeys, for these observers found that impairment of movement in a limb resulted on section of the sensory roots of the spinal nerves supplying the limb.

If the interruption of afferent impulses in their passage through the sensory nerve roots is capable of producing impairment of movement, there is no reason why the interruption of similar afferent impulses passing up the lateral region by the medulla and in the inferior cerebellar peduncle should not be also capable of bringing about a similar result.

That this is probably the correct explanation of the way in which defective movement is brought about by division of one inferior peduncle or by lateral section of the medulla is suggested by the fact that the degree of sensory and motor impairment in the limbs is very much alike, that is, the limb in which motor power is most defective after these lesions is that in which most sensory impairment was met with, while that in which there was least sensory impairment was that in which there was least defect of movement. It is further significant, in this connection, that improvement in sensory conduction could always be detected before there was any sign of improvement in motor power in these animals.

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* CLAUDE BERNARD, "Leçons sur la Physiologie et la Pathologie du Système Nerveux."

† MOTT and SHERRINGTON, 'Roy. Soc. Proc.' 1894–5, Vol. 57, p. 481.

If the above is the true explanation of the way in which motor paresis is brought about by lateral section of the medulla or division of the inferior cerebellar peduncle, these results, taken in conjunction with those in which the posterior columns and their nuclei were divided, make it probable that the path of the afferent impulses whose interruption in the sensory roots is capable of causing impairment of movement is by way of the direct cerebellar tract rather than by the posterior columns.

That the cutting-off of some afferent impulse is responsible for the ocular displacements seems clear. It is interesting to note that such impulses appear to have two paths from the periphery, in that interruption of both the direct cerebellar tract and the posterior columns results in ocular displacements, though in the former case, as in division of the inferior peduncle of the cerebellum, the eyes are displaced away from the side of the lesion, with the displacement most marked in the opposite eye, while in the latter case the eyes are displaced to the side of the lesion, the displacement being most marked in the eye on that side.

It is curious that the ocular displacements which result from section of the inferior cerebellar peduncle should differ so widely from those which follow section of the auditory nerve, after which lesion the eye on the same side rotates downwards and inwards (towards the opposite side), or sometimes outwards (to the side of the lesion), while the opposite eye, in which there is most displacement, and which rotates downward and outward after section of the peduncle, in the case of the auditory nerve turns inward, and, according to BECHTEREW,[*] also upward.

The fact that the direction of displacement of the globes which results from section of one inferior peduncle of the cerebellum, is the same as that which results from ablation of one lateral half of the cerebellum, opens up the question as to whether the latter displacement is not also an indirect effect rather than one due to the taking-off of a direct influence normally exerted on the ocular muscles by the cerebellum.

With regard to nystagmus, nothing need be added here to what was said in my former paper.[†]

The spasm which was so easily detected in the back and neck muscles on the side of the lesion alone furnishes us with any satisfactory information with regard to the possible control which the cerebellum may exert on the spinal centres, an action which seemed highly probable from the results which were met with after ablation of one lateral half of the cerebellum. No reliable conclusion can be arrived at in connection with the spasm in the limbs, which was not of the very pronounced character such as was met with after cerebellar ablation, and which, therefore, was difficult to distinguish from voluntary contraction of the muscles by the animal.

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[*] BECHTEREW, 'Pflüger's Archiv,' 1883, Vol. 30, p. 312.

[†] *Loc. cit.*

More disappointing still was the absence of evidence from the state of the tendon reflexes, for from their condition of exaltation after ablation of the cerebellum, it seemed likely that they would furnish still more definite information with regard to the question of control of the cerebellar over the spinal centres, when the inferior cerebellar peduncle was divided on one side; instead of which anything approaching the degree of exaltation of the tendon reflexes met with in the former experiments was never observed, and while the evidence on the whole pointed to the knee-jerk on the side of the lesion being slightly more increased than that on the opposite side, this was a question about which there was always a good deal of doubt.

While the state of the reflexes furnishes no satisfactory evidence in support of the view that the cerebellum exerts a control over spinal centres, the reflexes certainly do not supply any evidence to strengthen the view that this organ reinforces the spinal centres, for in no instances was there any diminution, much less abolition, of the tendon reflexes after section of one inferior cerebellar peduncle.

The blunting of sensibility met with is further proof that the cerebellum is concerned with sensory as well as motor processes, as was contended in my former paper. It is also important to find that the distribution of the sensory impairment after section of the inferior peduncle is the same as after ablation of one lateral half of the cerebellum.

Important as are many of the results that have already been discussed, none are more important, and few as interesting as those obtained on comparing the electrical excitability of the two cerebral hemispheres after section of one inferior peduncle, or after partial hemisection of the medulla. From the increased excitability of the cortex of the opposite cerebral hemisphere met with after ablation of one lateral half of the cerebellum, I concluded that the one half of the cerebellum normally exercised a control on the opposite cerebral cortex; it is therefore gratifying to find this view further supported by the results now under discussion. The fact that with all the cerebellar centres intact, and with the paths by which impulses may pass to the cerebral hemispheres also intact, section of one inferier peduncle of the cerebellum is followed by a lesser degree of excitability of the cortex of the opposite cerebral hemisphere, as compared with that of the hemisphere on the same side, suggests the possibility that the influence of control exerted on the opposite cortex by the half of the cerebellum whose inferior peduncle is divided, is heightened by the taking-off of some afferent inhibiting influence, normally acting on this half of the cerebellum, and reaching it by way of the inferior peduncle.

This view is strengthened by the remarkable results obtained by the intravenous injection of absinthe in animals in whom the same lesions had been previously produced. That with the pyramidal system absolutely intact from the cortex to the spinal centres, and that with the path from these to the muscles of the fore-limb on the side of the divided cerebellar peduncle also intact, there should be an entire absence of contraction of the muscles of this fore-limb, at a time when all the other muscles of the animal are engaged in the general convulsions, induced by the drug, seems hardly credible, but is nevertheless the case. The only ways in which such an effect could be accounted for are, either by supposing that in order to reach the muscles of the limb in question the epileptic spasms generated in the cerebral cortex have to pass through the cerebellum to reach the spinal centres by way of the inferior cerebellar peduncle, which being divided prevents the impulses from passing; or we must admit that some afferent inhibiting influence has been taken off the half of the cerebellum whose inferior peduncle has been divided, and that this allows this half of the cerebellum to exert an influence on the opposite cerebral cortex sufficiently inhibitory in character to prevent the centres from being discharged by the absinthe. From what we know of the way in which impulses are conducted from the cerebral cortex to the periphery, there seems little likelihood that the former of these explanations is the correct one; while the evidence at our disposal on this point makes it probable that the latter is the correct explanation of the mode of production of the phenomena under consideration.

That the muscles of the posterior extremity on the side of the lesion contract, though less powerfully than do those of the opposite limb, is evidence that the same degree of control is not exerted on all the centres of the opposite cortex; but it is also possible that some of the spasm in the muscles of the posterior extremity on the side of the lesion may originate in the cerebral cortex of the same side as the limb.

The way in which the convulsions are diminished, and tonus largely replaces clonus during the muscular contractions which take place in the anterior extremity on the side on which the posterior columns and their nuclei have been divided, are interesting points, as is the fact that these differences become more pronounced after a series of convulsions; but in dealing with so much that is unfamiliar, it appears to me to be better to record the facts without at present entering into any speculations as to their significance.

III. *The Menstruation and Ovulation of Macacus Rhesus, with Observations on the Changes undergone by the Discharged Follicle.*—Part II.

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Communicated by Professor M. FOSTER, *Sec. R.S.*

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[PLATES 1, 2.]

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Introduction.

THE greater part of the material wherewith the work detailed in this paper was done, was obtained during my stay in Calcutta during the early part of 1891, and I am greatly indebted to the Committee of Management of the Calcutta Zoological Gardens, and especially to Professor D. D. CUNNINGHAM, F.R.S., both for assistance in getting the animals required and for facilities placed at my disposal for carrying on my work in that country.

Two hundred female *Macacus rhesus* were sent to me from Muttra and thirty from

Benares. A very large proportion of these either had embryos in an advanced stage of development in utero, or had recently borne young; of the remainder many had not yet reached the age of puberty, and when all doubtful cases were excluded, seventeen specimens alone remained which could be used for the purpose of investigating the phenomena of menstruation. Five of these were referable to Stage 1, the resting or intermenstrual stage, and the other twelve to various stages of the menstrual cycle.

Great care was taken to exclude all animals about which there was any doubt either as to perfect health, premature abortion, or recent delivery. The size of the uterus and the condition of its muscular coat, the consistency of the walls of the os uteri and whether or not it was dilated, and the condition of the mammary glands, were specially noted.

Besides the material collected in Calcutta, eight female *M. rhesus* were kept by me for three to fifteen months in Cambridge, in a building heated with hot water pipes during the winter, and the menstruation of these animals was noted at various times; the climate, however, appeared to affect their health, and the results obtained cannot be considered satisfactory.

Anatomy of the Cervix.

With the exception of the cervix, the anatomy of the generative organs of *M. rhesus* is very similar to that described for *Semnopithecus entellus* in Part I. of this paper. The cervix, however, is different.

In *S. entellus* the cervix is a narrow straight canal with thick muscular walls. In *M. rhesus* a fold is formed on the anterior (ventral) wall, which projects across the lumen of the canal of the cervix and fits into a recess between two similar folds formed on the opposite wall, the whole constituting, as it were, a valve between the internal and external os uteri (figs. 3 and 4).

The canal at this intermediate point is thus rendered very narrow and convoluted; from the valve to the external os it widens out somewhat laterally and ends as a small slit on a papilla projecting into the vagina, while from the valve to the internal os it also becomes enlarged and enters the uterus by a wide mouth. The wider portions of the cervix canal have longitudinally folded walls, but in the intermediate valvular portion the folds are not present.

The position of the internal os is readily determined; the folded walls of the mouth of the cervix end abruptly at the point where the uterine cavity begins, and histological examination shows a distinct difference between the two parts; further, the various changes, which are so marked in the uterine mucosa during menstruation, do not extend to this portion of the generative canal.

The valvular structure is not confined to virgins; it is present in a specimen in my possession which has borne young, it is therefore a permanent structure.

I am not aware that this peculiar valve in the cervix canal exists in any other animal, and what its function may be I am quite unable to say; it probably serves to prevent the escape of the seminal fluid which has once been drawn into the uterus, but it is not likely this is its sole use.

Breeding and Gestation.

It is remarkable how little is known of the breeding habits of monkeys. In India, where several species abound close to native villages at all times of the year, it might be expected that their habits at least should be well known.

BLANDFORD (No. 1), in his recent work on the Fauna of British India, says there is no particular breeding season for *M. cynomolgus*, but I can find no other reference to the subject in his book.

Mr. SÁNYÁL, Superintendent of the Zoological Gardens at Calcutta, told me it was his opinion that *M. rhesus* bred at all times of the year. No doubt he has received individuals which have borne young at widely different seasons, and it was this fact, I believe, which led him to adopt his view; but that fact, in itself, is no proof that the animals breed at all times of the year in all parts of the continent of India. The specimens received at the Gardens may have been obtained from different parts of the country, where climatic and other conditions (such as food) are very different, and this circumstance would be quite sufficient to account for the widely different seasons during which the young are born at the Gardens.

Dr. AITCHISON has informed me that in Simla *M. rhesus* copulates about October and gives birth about August and September the following year. Apparently, then, these animals have a definite breeding season in Simla.

My own investigations show that the *M. rhesus*, which live on the plains about Muttra, breed at a different time of the year, and yet that they also have a definite breeding season.

The fact that a very large proportion of the adult females supplied to me during January, February, and March, bore advanced embryos in utero, and further, the fact that of those supplied in March a very large proportion had already borne young, points to the conclusion that March is the usual month when most of the young are born at Muttra.

Thus it is seen that the breeding season in Simla and in Muttra occurs at quite different times, and it would seem highly probable that *M. rhesus* living in other parts of India, may have different breeding seasons also. The geographical range of this species is very great, it is found over an area bounded by Kashmir (latitude 34) to the Godavari River (latitude 17), from Bombay (longitude 73) to Bengal (longitude 90), from an altitude of nearly 10,000 feet down to near sea-level;* and the conditions, both of climate and of food, over this wide area, are surely various enough to account for all possible variations in the breeding time.

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* See BLANDFORD (No. 1).

The period of gestation of *M. rhesus* is also by no means certainly known. **Breschet** (No. 2), who gives a fuller account of the observations which have been made on this subject than any other author with whom I am acquainted, quotes a statement made by **Isidore Geoffroy Saint-Hilaire**, to the effect, that it is agreed to fix the duration of the gestation of apes at about seven months. He himself does not, however, appear to agree with this view, for after detailing the observations of other naturalists, he asserts that the period of gestation varies in different species, a conclusion which it seems to me he is justified in drawing.

With regard to *Macacus*, he remarks that **Frédéric Cuvier** believed it possible to determine the gestation of "Maimon" (*M. nemestrinus*) at seven months, twenty days.

Breschet shows that, unlike many of the lower mammals, monkeys frequently indulge in sexual intercourse, not only at the breeding season, but also during pregnancy; and further he records F. **Cuvier**'s observation, that menstruation takes place not infrequently during pregnancy. These facts make it doubly difficult to determine accurately the duration of gestation, and undoubtedly further investigations are required on this point.

Blandford (No. 1) states for the genus *Macacus* that the period of gestation is about seven months, and that the gestation of *M. nemestrinus* has been ascertained to be seven months and twenty days, but he gives no reference to the source from whence he got his information.

The account Dr. **Aitchison** gives me of *M. rhesus*, at Simla, deals only generally with the breeding season and the time of bearing young; but, from his observations, it would seem to be not improbable that the gestation of this animal occupies considerably more than seven months' time.

The fact that there is a definite breeding season for these animals, if it be true (as I cannot but think it is), conveys of course no proof that each female breeds each year.

The only evidence which I have to record which bears on this point, is the fact that menstruation undoubtedly occurs while the mother is nursing her young.

I have noted for three months the occurrence of very regular menstrual periods in the case of a specimen of *M. cynomolgus*, which was nursing a young one at the time. It is true the mother did not supply all the nourishment the young one took, but I think I am right in saying she supplied most of it.

It would seem possible therefore that the female monkey may become pregnant during the period of lactation, more than this I cannot say.

There is some reason for the suggestion that the act of copulation is dependent, quite as much upon the condition of the male, as it is upon the condition of the female. I have seen female *Semnopithecus entellus* endeavour to induce a full grown male to fertilise them without success, and this occurred at a time of year which, I was told, was somewhat less than a month before the usual breeding season began.

Menstruation.

With regard to the regularity of menstruation in Monkeys, it seems advisable I should add a word to what I have already said in Part I. of this paper (No. 8).

There is considerable evidence in favour of the view that certain monkeys menstruate regularly all the year round. **Geoffroy Saint-Hilaire** and **Cuvier** (No. 7) found that in three different species, Cercopithecus, Cynocephalus, and Macacus, there was a regular monthly discharge of blood from the generative organs. **Sutton** (No. 17) states that the specimens of *M. rhesus* which he investigated, and which I understand he obtained from the Zoological Gardens in London, menstruated fairly regularly; while Mr. **Bartlett**, Superintendent of the Zoological Gardens in London and Mr. **Sányál**, Superintendent of the Gardens in Calcutta, have both assured me that monkeys menstruate regularly in their establishments.

A specimen of *M. cynomolgus* which I observed in the Gardens at Calcutta for three months menstruated regularly during that time, a bloody discharge exuding from the vagina on 20th December 1890, 20th January 1891, and about the 20th February 1891.

A specimen of *Cynocephalus porcarius* which I also noticed in the Calcutta Gardens for two months, menstruated regularly for that period, while the specimens of *Semnopithecus entellus* which I kept for observation in Calcutta, menstruated each month and the flow from the vagina lasted about four days.

The specimens of *M. rhesus* which I kept in Cambridge, were not all adults at the time they were sent to me, two of the adults, however, menstruated regularly for the three months during which they were under observation. In these animals the flow was observed to last for three to five days, and the probable mean dates were:

Specimen A. 7th May, 1892; 2nd June, 1892; and 6th July, 1892.
,, B. about 11th May, 1892; 11th June, 1892; and 6th July, 1892.

After this date until the end of the year, specimen B was irregular; she generally was found to have a secretion exuding from the vagina but it was rarely tinged with blood.

A third specimen suffered much from cold and cough and rarely menstruated, two others died, two were young ones which did not menstruate at all, and the eighth menstruated irregularly.

External Signs of Menstruation.

Apart from the menstrual flow, other signs were observed which regularly recurred with menstruation in *M. rhesus* and *M. cynomolgus;* the nipples and vulva became swollen and deeply congested, and the skin of the buttocks swollen, tense, and of a brilliant red or even purple colour; the abdominal wall also, for a short space upwards, and the inside of the thighs, sometimes as far down as the heel, and the under surface of the tail for half its length or more, are all coloured a vivid red; while the skin of the face, especially about the eyes, is flushed or blotched with red.

Professor SHERRINGTON has made similar observations on *M. rhesus*, and has very kindly supplied me with sketches showing the extent of the area of skin in the neighbourhood of the generative opening, which he found to be so affected. His results agree in the main with those I have described above for the buttocks, hind limbs, and tail; but I gather from his coloured drawings, that the congested area in the animals he observed (they were kept in London), was neither so brilliant nor quite so extensive as that seen by me in specimens which lived at the Gardens in Calcutta.

This congestion of the skin of the buttocks, thighs, and tail is also observed in females during, at any rate, the later stages of gestation; but in such animals the area of the abdominal wall which is affected, is larger than it is during menstruation, and the intensity of the colour of this part is considerably increased. The colour of the face during this later period of gestation, is also more brilliant than it generally is during menstruation. So marked is the former difference that a pregnant monkey from about the period of the fifth month of pregnancy, although not always readily distinguishable by its increased size, can be surely determined by observation of the extent of the congested area of the abdominal skin.

Nor is the brilliant colouring of these parts confined to the female *M. rhesus*. The males, when adult, are also brilliantly coloured in the region of the buttocks and over the face. For the three months during which I had them under observation, I could see little or no difference in the degree of intensity of the colouring, but whether this is a permanent characteristic of the male or not, I am unable to say.

The innervation of this congested area, which is of very considerable interest, I have drawn attention to in my former paper (No. 8).

The Menstrual Discharge.

The nature of the menstrual discharge from the vagina varies little, from time to time, in any one individual, as far as I have been able to discern during the few months in which I have had an opportunity of examining it; and, further, the same may be said for different individuals.

The discharge consists of:—

(1.) A somewhat viscid, stringy, opaque, white fluid. The fluid itself is transparent, and is, I believe, derived from blood serum and from the glandular cells of the uterine mucosa. The opacity of the fluid is due to the presence of great numbers of minute granules; these have their origin chiefly from the broken down plasmodium which constitutes the bulk of the uterine mucosa. At the same time, some of the nuclei of the cast-off uterine tissues, especially the glandular epithelium nuclei, and also degenerate leucocytes, give rise to granules. I have obtained fresh material from the uterine cavity of a menstruating monkey which shows these facts.

The glandular fluid itself, when present in the lumen of the glands, contains granules in small numbers which are apparently excreted by the glandular cells. Sometimes the discharge is more fluid, at others more viscid; sometimes it is more, sometimes it is less opaque, but the variations are not very great.

(2.) Red blood corpuscles. These are invariably present in quantities sufficient to colour the discharge either a pale or a dark blood colour; the latter, however, is rare.

(3.) Masses of uterine stroma tissue, pieces of uterine epithelium, both from the wall of the uterus and from the uterine glands, together with squamous epithelium from the vagina.

(4.) Leucocytes sometimes, though not generally, in large numbers, and the isolated degenerate nuclei of broken down epithelial cells and stroma tissue. The quantity of these nuclei of the uterine tissues is various; I have seen them in very large numbers in some specimens of menstrual discharge, while in others they occur rarely.

The menstrual clot is formed of a mass of blood corpuscles, together with pieces of the various uterine tissues which are cast off by the menstrual process; it is expelled apparently at the end of menstruation, and is found in the uterine cavity in varying degrees of solidity according to the length of time it has remained there.

The variations observed in the composition of the normal menstrual discharge, may be due either to the stage of menstruation during which the specimen was obtained, or to a variation in the manner of menstruation itself.

My histological investigations of the uterine tissues during menstruation, show the remarkable uniformity of that process in the numerous specimens examined, and make it extremely unlikely that such variations as are seen in the composition of the normal menstrual discharge, should be due chiefly to variations of the manner or extent of menstruation. On the other hand, it will be readily understood that a variation in the number of leucocytes, for instance, may be accounted for by the stage of menstruation in progress at the time the specimen was taken. When the uterine epithelium first ruptures, and the mass of blood corpuscles and fresh leucocytes contained in the large lacunæ are expelled into the empty uterine cavity, the discharge will contain little else; but later, when a mass of uterine tissue occupies the cavity of the uterus, the easy flow is no doubt retarded, and disintegration of all the cellular material, epithelium, stroma, and leucocytes will take place, and will cause the discharge to assume a more viscid and more granular appearance.

Leucorrhœa.

One monkey which I kept in Cambridge, suffered, at the time I got her, May, 1892, until I killed her, August, 1893, from a discharge from the vagina other than a menstrual discharge. It occurred at first irregularly, gradually, however, it became more frequent, until eventually it was almost continuous.

This discharge had the appearance of a more or less viscid, more or less opaque white material, and consisted of a dense granular fluid in which great numbers of squamous epithelial cells were invariably present. Besides these cells there were at times a considerable number of eosinophile leucocytes, which, in some cases, contained four or more nuclei, and were therefore, according to **Flemming**, breaking down; these leucocytes were most numerous when the fluid was most viscid and thick. There were no free red blood corpuscles and no cast-off uterine tissue was to be seen; the cellular contents of the fluid, other than leucocytes, were derived entirely from the vagina and not from the uterus. The fluid itself, on the other hand, came chiefly, at any rate, from the uterus.

When the animal was killed, the vagina was full of this white, opaque, viscid fluid, and so was the cervix within the external os, while much was also found in the cavity of the uterus itself and some in the lumen of the uterine glands.

No doubt the discarded vaginal epithelium when it breaks down gives rise to a certain amount of viscid granular fluid, but as there are no glands within the vagina it is only by the former means that fluid can be formed therein, by far the greater part therefore of the fluid portion of this discharge came from the uterus. It was noticeable that the fluid contents of the glands in this specimen, contained considerably more granules than were to be seen in the glands of specimens of menstruating uteri.

In spite of this abnormal discharge, which I take to be leucorrhœa, this monkey was especially healthy and strong.

It never menstruated while I had it, but the buttocks, face, and mammæ were frequently congested, sometimes remarkably so.

On examination after death the ovaries were found to be undergoing atrophy. In one of them the external tunic of the ovary was thickened and separated from the internal stroma, while the latter had shrunk away and appeared like the kernel of a nut inside its husk, the other ovary was similarly affected, but not to the same extent.

Superficial Menstrual Phenomena.

The same grouping of menstruating uteri is adopted in the present paper as that recorded in Part I. of this work (No. 8), on *Semnopithecus entellus*, viz.:—

A.	Period of rest	Stage I.	The resting stage.
B.	„ growth . . .	„ II.	The growth of stroma.
		„ III.	The increase of vessels.
C.	„ degeneration .	„ IV.	The breaking down of vessels.
		„ V.	The formation of lacunæ.
		„ VI.	The rupture of lacunæ.
		„ VII.	The formation of the menstrual clot.
D.	„ recuperation .	„ VIII.	The recuperation stage.

A superficial examination of the mucosa of the menstruating uteri of *M. rhesus* shows that changes take place in them which are similar to those described for *S. entellus.*

The smooth surface of the mucosa during Stage I. becomes more opaque during Stage II., and the flush which spreads over the mucosa during Stage III. gets more and more marked, until at the end of Stage IV. the mucosa may be said to be highly congested. At Stage V. the dark red spots appear on the surface of the mucosa, which are characteristic of this stage, and which are due to the formation of lacunæ, while at Stage VI. free blood is first seen in the cavity of the uterus. The formation of the menstrual clot during Stage VII., and the recuperation of the uterine mucosa during Stage VIII., are also superficially the same in *M. rhesus* as they are in *S. entellus.*

Histology of Menstruation.

The account, given below, of the histological phenomena exhibited during the menstruation of *M. rhesus* is very brief. Similar work has been undertaken for *M. rhesus,* which I have already described for *S. entellus* (No. 8). A large series of specimens have been examined in the form of serial sections, and the various phenomena compared, step by step, with those exhibited by my preparations of the menstruating uteri of *S. entellus,* and a close similarity between the two has been found to exist. While it has been thought advisable to note the points of agreement and difference, which are brought out by an examination of the process of menstruation in these two species of monkeys, and to point out the fact that the results arrived at by the study of *M. rhesus,* entirely confirm the results which my examination of *S. entellus* led me to publish, I have purposely avoided all unnecessary repetition, and have been obliged, in consequence, to assume some knowledge of the details given in Part I. of this paper (No. 8).

The advisability for this course has seemed to be the more pronounced since the results which I have arrived at differ, in various important particulars, from the accounts of menstruation which have been generally accepted, and a confirmation of the former has therefore some increased interest and importance.

With regard to the body of the uterus, I have only here to record the fact that the mucosa is somewhat thicker than it is in *S. entellus*, and that the protoplasmic network of the stroma is more granular and is denser, and the glands more numerous and more branched than are these structures in the latter animal.

In *M. rhesus* as in *S. entellus*, there is an absence of any connective tissue framework in the stroma; we have, in fact, here, an essentially primitive tissue capable of extensive and rapid growth, and of transformation into other and more specialised tissues. The uterine and glandular epithelium, the glands devoid of a definite sheath, and the arrangement of the musculature, are all the same as are seen in *S. entellus*.

A. *Period of Rest. Stage I.*—The nuclei of the stroma at this stage are more densely packed in the lower portion of the mucosa than they are in the superficial part; in the latter situation a loose tissue exists, held together by a network of delicate protoplasmic processes.

I have observed no fibrils in the stroma of *M. rhesus*.

B. *Period of Growth. Stage II.*—There is a great increase in the number of the nuclei of the stroma, by means of amitotic division, in the upper third of the mucosa. The layer becomes in this part very densely crowded with nuclei, which, owing to the restraining pressure of the epithelium above, become elongated and flattened; they continue to exhibit great activity in division and growth. Thus hyperplasia occurs. The rapidity with which division goes on may be judged of by the proportion of very small nuclei present; they have their origin from the products of the first division of the stroma nuclei, and are in much larger proportion than the parent kind in many parts of the growing stroma layer.

Two methods of division of the nucleus occur, namely division into two and fragmentation.

The elongated nuclei of the growing stroma become constricted and divide into two, they are constantly to be seen in various stages of this process (fig. 1, Plate 1).

Division by fragmentation in the case of the nuclei of the stroma, I laid some stress upon in my former paper (No. 8), but was unable to demonstrate, to my own satisfaction, the actual separation and isolation of the various portions of the fragmented nucleus.

The same difficulty of demonstration occurs also in *M. rhesus*. Owing to the crowding together of the nuclei into what is almost a compact mass, and owing to the continuous network of protoplasm, at this stage becoming practically a solid layer without meshes and without connecting processes, I have found it impossible to prove satisfactorily the origin of separate nuclei by fragmentation. Fig. 2 will serve to show the nature of the difficulty. This drawing is made with REICHERT'S one-fifteenth immersion lens and ZEISS' No. 4 eye-piece, and it is, as nearly as I can make it, exactly similar to the actual specimen, the nuclei are very small and the scanty protoplasmic matrix is entirely devoid of cell outlines. The group of nuclei marked *a*, in which three nuclei are indicated still attached the one to the other, I interpret to be a nucleus undergoing fragmentation, while the groups of nuclei marked *b*, *c*, in which three nuclei are seen closely allied to one another, seem very probably derived from fragmented nuclei, although it is impossible to be quite certain of the fact owing to the nature of the protoplasm, the crowding together of the nuclei and the absence of cell walls.

The growth of stroma tissue described above, causes a swelling into the lumen of the uterus and the thickness of the mucosa is in this way increased.

When the nuclei, which I believe to be formed by fragmentation (fig. 2), are compared with those which are formed by division (fig. 1), the size of the former will be seen to favour the view expressed. Both these figures are drawn on the same scale, and it is clear that the group of nuclei in fig. 2, marked *a*, are certainly not larger than a single nucleus of the dividing cells show in fig. 1.

Stage III.—The vessels increase in number and size, and leucocytes are more numerous therein than they were in the former stages.

C. *Period of Degeneration. Stage IV.*—No sign whatever of fatty degeneration was observed; hypertrophy, followed by degeneration of the walls of the vessels, results in the breaking down of the vessels and the escape of the blood into the meshes of the stroma tissue.

The degeneration changes are confined to the superficial part of the mucosa, while the hypertrophy is seen all through the mucosa, both in the cells forming the walls of the vessels and in the stroma tissue itself.

There is an increase in the number of leucocytes within the vessels throughout the whole of the mucosa, but no free wandering leucocytes were found in the deeper portion of the layer; they were only to be seen in the region of the broken-down vessels. Diapedesis does not take place, and it may, therefore, be assumed, that the element which the leucocytes have been summoned to attack is present within the vessels, and is not in the surrounding tissue (see Part I., p. 429).

Stages V. and VI.—Small lacunæ are first formed in the superficial stroma; they increase in size as more and more blood is poured into them, and eventually they come to lie directly below the epithelium. Eventually the epithelial layer ruptures, and the blood is poured into the uterine cavity.

Degeneration of the nuclei of the uterine epithelium and superficial stroma also takes place during this period, and is very marked during Stage VI.

The number of leucocytes is very largely increased.

Stage VII.—I have nothing to add to the description of the mucosa menstrualis already given in Part I. of this paper (No. 8). Denudation occurs in *M. rhesus* as in *S. entellus;* it is brought about in a similar manner and exists to a similar extent; a menstrual clot is also formed in the same way.

I have here very conclusive confirmation of the truth of the account given for *S. entellus.* Fig. 8, Plate 37, in my former paper might, in fact, fairly represent my specimens of the same stage in *M. rhesus.* The denudation is a remarkable process; both its completeness and extent are unquestionable.

D. *Period of Recuperation. Stage VIII.*—An account of this stage resolves itself into a repetition of what I have already written with regard to *S. entellus.*

The epithelium is re-formed, partly from the epithelium of the glands which remain *in situ*, and partly from stroma tissue.

New vessels are also formed from stroma tissue, by means of which all the blood corpuscles, included within the newly formed epithelium, are drawn again into the circulatory system.

In the deeper part of the stroma, the cells forming the walls of the hypertrophied vessels become again of normal size and consistency, and the stroma tissue is also reduced in bulk, assuming again the conditions which are found during the resting stage.

With regard to the leucocytes, I have no further evidence to offer; I would merely say that the opinion I have already expressed with regard to their presence during the menstruation of *S. entellus*, is confirmed by the observations I have made on *M. rhesus.* If METCHNIKOFF's conclusions are to be relied upon, the presence of leucocytes in such large numbers in the vessels of the mucosa during menstruation, is evidence of a noxious material therein, while the fact that diapedesis does not occur, shows that the irritant does not extend to the surrounding tissue. Menstruation, then, cannot be considered to be an inflammatory process.

The considerable flow of blood from the ruptured vessels during menstruation would seem to get rid completely of this irritant, and this is itself sufficient to explain the disappearance of the comparatively few leucocytes which are left after denudation has taken place.

Menstruation in the Human Female.

Owing to an oversight, I omitted to draw attention in my former paper to the fact that MINOT (No. 13) divides the act of menstruation into three periods, which he calls

1. Tumefaction;
2. Menstruation;
3. Restoration of the mucosa;

and he distinguishes between these periods and a period of rest which completes the menstrual cycle.

These four periods are identical with those I have independently adopted, but the terms he has used to designate the first two of them do not appear to me to describe sufficiently accurately what takes place.

MINOT's period of "tumefaction" must include also that most important preliminary phase which I have described as "growth of the stroma"; from my point of view, the omission to recognize this as a primary division is an error which goes to the root of a proper understanding of the forces, whatever they may be, which cause menstruation; for I hold there is no doubt that a period of growth precedes the increased supply of blood which subsequently flows to the mucosa, and that it is to the forces which bring about this growth we must look for a solution of the origin of the process of menstruation.

Then again, MINOT's term "menstruation" omits to include the degenerative processes which occur prior to the appearance of the menstrual flow, and it seems to me important that this degeneration should be recognized as a distinct phase of the process.

MINOT describes an infiltration of blood from the vessels—no rupture of vessels at this stage having in his opinion been proved—and subsequent degeneration of the superficial layers of the mucosa, but he thinks the degenerative process is of later occurrence than the bleeding, and that it does not cause the bleeding. Here my results differ from the views this author has adopted, and it may be, that it is this difference of opinion which has prevented him from placing so much stress upon degeneration as I have done.

MINOT's description of a normal virgin uterus near the close of menstruation, and his figure of the same, though the latter is on too small a scale to admit of close comparison, show a great similarity to the description and figures given in my former paper on *S. entellus*, and give increased force to the view that, broadly speaking, the process of menstruation in man and in the monkey are practically identical.

MARTIN's article (No. 12) to which I was unable until recently to obtain access, should also be noted. He states that before the menstrual flow occurs a growth of the middle layer of the mucous membrane takes place, causing it to become five or six times thicker than before, that the lymph channels and glands become wider, that the blood-vessels become gorged and some burst, and that blood finds its way into the cavity of the uterus either by extravasation or by diapedesis, adding that possibly both, but probably the former, of these processes occur. After the blood has passed out, he says, the mucous tissue breaks down, fatty degeneration occurs, and more or less of the uterine coat is thrown off.

Here, then, we have periods of growth and of degeneration; of the former of these MARTIN's description is similar to the one I have given for monkeys, but with regard to the latter there are some differences, namely, he is of opinion that firstly, the mucous tissue breaks down only after the passage out of the blood, while I show in monkeys that degeneration occurs before the blood flow begins; and secondly, that fatty degeneration occurs, whereas I can see no trace of it.

JOHNSTONE (No. 9) reiterates the opinions he published in an earlier paper, with which I have already dealt in Part I. of this work.

CHAMPNEYS (No. 3), in an able work which escaped my attention until recently, points out that the investigation, by the histologist, of the phenomena of menstruation in the human female, necessarily neglects the peculiarities of the individual. It would seem by no means improbable, that these peculiarities are sufficiently great to cause many of the diverse views held by various investigators, who have not been able to examine a very large number of specimens, and there is no doubt **Champneys** is right when he states, that the observation of the histologist needs controlling and correcting by clinical observations.

This author seeks to show that, possibly, the menstrual flow may be determined by uterine contraction acting suddenly upon a swollen mucosa, the vessels of which are distended with blood.

I am not disposed to argue that uterine contraction does not take place during the active menstrual time, but if my observations upon the degeneration of the walls of the vessels, and of the mucosa generally, are true, and if an extravasation of blood such as I have described in the case of monkeys, also takes place in the human menstruating uterus, it follows that the menstrual flow is not dependent upon uterine contractions.

Although no doubt such a force would materially assist in the ejection, from the uterus, of the mucosa menstrualis, it must be remembered that muscular contraction of the uterus will decrease the actual flow of blood, not increase it (see Part I., pp. 436–7).

The Re-formation of the Uterine Epithelium.

I have come to the same conclusion with regard to the re-formation of the uterine epithelium after menstruation, as I detailed in Part I. of this paper. Some portions of the new layer are no doubt derived from the torn edges of the epithelium of the glands, but others, I feel confident, are derived from the elements of the stroma.

In this belief I find I am not so completely isolated as I had supposed, although many observers emphatically deny that such a process takes place.

Duval (No. 6), who has worked at the regeneration of uterine epithelium after delivery, comes to the same conclusion as I do. The idea of the transformation of "cellules conjonctives en cellules épithéliales," he says, was so repugnant to him that he for some time disregarded preparations which appeared to show this, and it was not until he had many preparations to study, that he convinced himself, that uterine epithelial cells are actually formed from the uterine stroma; of this fact he clearly states he has now no doubt, and he considered his evidence irrefutable.

Johnstone also (No. 9) believes the epithelium of the human uterus, which takes the place of that thrown off during menstruation, is regenerated, not from the remains of the old epithelial layer, but from the connective tissue structures which underlie that layer.

Kiersnowski (No. 10), on the other hand, denies the fact. He gives an historical account of the literature of the subject of the regeneration of epithelium, and a very complete list of papers. His own work was done upon the regenerating uterine tissue after delivery, of various animals, and he arrives at the conclusion, that the new epithelium is derived either from existing surface epithelial elements, or from the epithelium of the uterine glands. He points out, that in numberless places, flat epithelial cells can be demonstrated to be continuous with pre-existing columnar epithelia cells, either of the surface or of glands, and he denies that these flat cells are formed from the connective tissue cells below them.

There is no doubt **Kiersnowski** is quite right when he points out that much of the new epithelium is derived from pre-existing epithelial elements, but that in itself is no proof that all of it is so formed.

Duval's observations, and my own, show that certain connective tissue cells are transformed into epithelial cells, and I venture to think **Kiersnowski's** observations in no way disprove that fact. I would go further, and would point out that in many of the figures which he gives, the epithelium is shown to be already a continuous layer, and that it is not possible to determine from such specimens the actual origin of the cells.

Again, in fig. 2, he endeavours to show the forward growth of flat epithelial cells from cubical epithelial cells; this he does show, as I have also shown it in fig. 32 of my paper on *S. entellus* (No. 8); but there are in **Kiersnowski's** drawing, *also* superficial flattened cells which the author obviously intends to ascribe to this forward growth, since he shades them dark as he has done the cubical epithelium; but in my opinion, it is by no means clear that these cells are derived from pre-existing epithelial elements. The drawing is not very definite, and it stops short just at the point of interest, but it shows enough to incline me to gravely doubt the interpretation **Kiersnowski** has put upon his own preparations.

Strahl (Nos. 15 and 16) and **Noll** (No. 14) both follow in **Kiersnowski's** footsteps, and both lay themselves open to the same criticism. **Strahl's** figures are even less satisfactory than **Kiersnowski's**, as far as any proof of the origin of the new epithelium is concerned; indeed, I cannot discover that they carry any weight at all.

On the whole, therefore, while I do not deny that some new epithelium is derived from pre-existing epithelial cells, I hold that some is also formed from connective tissue cells, and I do not believe that the authors who combat this view have made out their case.

Ovulation in Macacus rhesus.

In Part I. of this paper the conclusions were arrived at: First that ovulation does not necessarily occur during each menstrual period, secondly that ovulation is not necessarily brought about by menstruation, and thirdly that the ripening of an ovum in the ovary is a process independent of the process of menstruation.

My observations on *M. rhesus* confirm these views. In consequence, however, of the very opposite views held by many investigators of this subject, it has seemed advisable to give some details here of the specimens which I have examined.

I do not propose to discuss in detail the formation of the so-called corpus luteum. During the last two years I have been engaged with a somewhat extensive series of experiments, upon the process of ovulation in the Rabbit; these seem to me to throw considerable light upon the subject, not only of the method of ovulation, but also regarding the formation of various kinds of corpora lutea; a detailed description of these experiments I hope to publish before long, here I will treat solely of the discharged Graafian follicles in *M. rhesus*.

Out of forty-three adult females of *M. rhesus* which were examined, twenty-two of them had no sign of a corpus luteum, or as I will call it a "discharged follicle," in either ovary; of these, fourteen were menstruating females, while the remaining eight were not menstruating at the time. On the other hand in twenty-one females a more or less prominent discharged follicle was present; of these, sixteen were pregnant females, or females which had very recently borne or aborted their young; while of the remaining five, one was a female which I am inclined to think had aborted her young, but I am not certain of the fact and consider this case doubtful (fig. 7), one was a non-pregnant, non-menstruating female (fig. 8), and three only were females in which menstruation was in progress at the time they were killed (figs. 5, 6 and 9).

Thus, out of seventeen menstruating females, three only were found, in the ovaries of which there was any sign of the existence of a discharged follicle. Of these three discharged follicles, one is undoubtedly the remains of a follicle long since discharged (fig. 5), it occurred in a female killed during Stage V. of menstruation; one is equally certainly, as I will show below, not of recent origin, it occurred in a female killed during Stage IV. of menstruation (fig. 6); and one only is a recently discharged follicle (fig. 9), and it was present in the ovary of a female killed during Stage VII. of menstruation.

Thus out of the seventeen menstruating females, in one case only was a recently discharged follicle found, and in that case only is it possible to say that ovulation and menstruation were coincident. I do not myself think that we are justified in asserting, even in this case, that ovulation and menstruation are coincident; of this point I say more below, but we are undoubtedly justified in saying, that in no other of the cases before us is there any possibility of asserting that these two processes are coincident.

The presence of ripe Graafian follicles was also looked for, and in one specimen only was a follicle found which could possibly be thought to be ripe. It was enlarged and somewhat prominent, but it appears to me impossible to be assured that it was in fact a ripe follicle, ready to discharge the ovum it contained. The female in which this was found was undergoing Stage V. of menstruation.

Passing now to a histological examination of a series of discharged follicles, a glance at the figs. 5 to 9 (Plate 1) will show the various stages which the discharged follicle passes through, on its way towards complete disappearance and amalgamation with the ovarian stroma tissue.

The first point which strikes one is the difference in the size of these discharged follicles. They are all drawn with the aid of a camera lucida, with the same object glass and eye-piece.

Omitting for a time fig. 9, the size of the other four is found to be in relation to, what I have for other reasons concluded is the comparative age of these structures.

Fig. 8 represents the most recent of the four, fig. 7 the next oldest, fig. 6 the next, and fig. 5 the oldest of the four.

The reasons which have enabled me to determine the relative age of these discharged follicles are set forth below, and are, briefly, the constitution of the material contained within the wall of the follicle and the condition of that wall itself.

I am not, however, disposed to consider the size of a discharged follicle an invariable guide to its age ; fig. 9 is in direct opposition to this view ; in this case the discharged follicle is of very recent origin, and yet it is smaller than that drawn in fig. 8, which represents a follicle which has been discharged some time before.

I draw attention to this question of the relative size, because the age of a "corpus luteum" has, by some authors, been determined by its size, and has led to considerable confusion. I would point out that, while in certain cases the size may be to some extent an indication of age, this is surely not an infallible guide in all cases.

I will first consider the most recently discharged follicle, shown in figs. 9, 14, and 15, obtained from an animal which was undergoing Stage VII. of menstruation when killed.

The discharged follicle is prominent, and the ovarian epithelium is attenuated where it covers the greater portion of the prominent part of the wall of the ovary, but is not present at all at the point x (figs. 9 and 15).

The contents of the follicle are not cellular, but consist of a network of densely granular material, and, with the exception of a very few odd isolated nuclei and a few scaered red blood corpuscles at the edge of the cavity, it contains nothing else (fig. 14). There is no sign of a blood clot.

The follicle wall is composed mainly of branched cells amongst which blood-vessels run (fig. 14), but, at its inner edge, these cells become longitudinally disposed and form a denser, almost fibrous inner boundary, which sharply separates the wall itself from the central cavity.

Blood-vessels are present both in the wall of the follicle and in the surrounding ovarian tissue, but they are larger and more numerous in the latter position.

The appearance of this follicle, as shown in fig. 9, its prominence on the surface of the ovary, and its pear-shaped central cavity, with the apex so nearly approaching the surface, indicates a recently discharged follicle. A more detailed examination of the point x and the neighbouring tissue, leaves no room for doubt that such is the case (fig. 15).

The ovarian epithelium, which is much flattened over the prominent swollen portion, is at the point x absent altogether, and from this point downwards to the apex of the follicular cavity, the tissue there existing is very much less dense and compact than is that of the rest of the ovary, while extravasated blood is present in this region, and is connected with a lacuna close to the surface of the ovary at x. This region seems to mark the line of rupture of the follicle, and, although one cannot say when the rupture took place, there seems good reason to believe it is of recent occurrence. The fact that this specimen was found in an animal which was menstruating at the time of death would doubtless, by many investigators, be considered sufficient evidence of the age of the structure, and it would, by such, be unhesitatingly asserted that in this case the follicle was ruptured during the act of menstruation then in course of progress.

It may be that this is the case, but I cannot admit that there is sufficient evidence of that fact. Here we have under consideration seventeen specimens of menstruating *M. rhesus;* in one of them, and in only one, a recently-discharged follicle is found; surely, then, very much stronger evidence must be adduced than is here obtainable before one can justifiably assert, that the actual date of the rupture of this follicle is in any way related to the act of menstruation going on at the time the specimen was obtained.

The second specimen is drawn in figs. 8 and 13. The animal from which this specimen was obtained, was not menstruating when it was killed, neither was it with young. It had been in my possession in Cambridge for fourteen months, and had not had access to a male during that time. It had suffered much from cold and cough, and had menstruated very irregularly while I had it.

In this case, also, the follicle is near the surface of the ovary, and forms a prominent swelling thereon. The ovarian epithelium, although much flattened, is, however, intact, and there is no evidence of the actual rupture of the follicle; at the same time there can be little doubt rupture has taken place in this case, and probably at no very distant date, at the point *y*. The wall of this follicle is much thicker than is the wall of the former specimen (fig. 9); hypertrophy has taken place; it is also characteristically folded, and contains blood-vessels. It is formed of branched cells, as in the case of the specimen just considered (compare figs. 13 and 14), but there is one prominent difference between the two: in the case now under consideration, in which hypertrophy has taken place (compare figs. 8 and 9), the inner boundary of the wall, instead of being more dense than the rest, is now irregular reticulated tissue, just like the rest (fig. 13); and, instead of being sharply defined, its cells are now continuous, with a loose wide-meshed network of cellular tissue, which now extends throughout the follicular cavity.

It would seem possible, that a certain amount of this interfollicular reticulated tissue is derived from tissue which grows in through the point of rupture, but there is abundant evidence to show that a very large portion of it, if not all, has its origin from the cells of the wall of the follicle. In every section the inward growth of these cells of the follicle wall is shown, and so also is their connection with the long-branched processes of the cells within the cavity.

There is no sign of a blood clot within the follicle; even isolated blood corpuscles are rarely met with, and only then close to the edge of the follicle wall.

The third specimen, drawn in figs. 7 and 12, shows a still further development. It is taken from a specimen, the history of which I am not quite certain about (see page 150), but for my present purpose it is of use, as showing an intermediate stage of the degeneration of the follicle.

The swelling on the surface of the ovary is not so pronounced as before, and the ovarian epithelium is formed of cubical cells. The follicular walls are more folded and the cavity smaller than before, while the blood-vessels are larger and more numerous, and exist now in the cavity as well as in the walls of the follicle. There is no blood clot, however, in the cavity of the follicle.

The cells of the wall are showing a change of arrangement; certain of them are becoming more rounded, and others are extending round these; the nuclei of the cells are noticeably reduced in size, and the tissue is more dense than it was in the second case. There is no longer any sign of hypertrophy.

The tissue within the small cavity of this follicle is also undergoing a change; the reticulated arrangement, seen in the cavity of the second specimen, is lost in this one, and minute branched nuclei, embedded in a homogeneous matrix, take its place.

Taken as a whole, this structure is smaller, and the tissue of which it is composed is denser than is the case in the preceding specimen.

The fourth specimen, drawn in fig. 6, was found in the ovary of a female which was killed during Stage IV. of menstruation. It is smaller than the previous specimen (fig. 7); the walls are less folded, and the central cavity is smaller, the blood-vessels, also, are fewer, and the whole structure lies deeper in the ovarian tissue.

The minute histology of this specimen shows similar advances. The tissue within the cavity of the follicle is now hardly to be distinguished from that composing its wall, and both are denser and more compact than has been hitherto described. Blood-vessels occur only in reduced numbers in the wall and in the tissue occupying the centre of the follicle, and they are also smaller than those seen in fig. 7.

If further evidence be required to prove that this follicle is of greater age than the one previously described, it is to be found in the occurrence of young Graafian follicles, each of which contains an ovum, which are situated between it and the surface of the ovary. These young follicles have no doubt been developed since the older follicle was discharged.

Finally, in figures 5 and 11, the fifth specimen is represented. The animal from which it was obtained I kept for some months in Cambridge; it menstruated regularly in May, June and July of 1892, and was killed in the latter month while undergoing Stage V. of menstruation.

The remains of this discharged follicle, the only one to be found in either of the ovaries, caused a slight swelling on the surface of the ovary, although the ovarian epithelial cells were not stretched and retained their usual cubical form. No central cavity is visible in this specimen, and no trace of the folded walls present in those previously described, is present in this one. A nearly solid mass of tissue (fig. 11), in the midst of which here and there a few blood-vessels run, is all that remains of the follicle.

The cells of which it is composed scarcely differ from the cells of the ovarian stroma, and consist of polyhedral cells or multinucleated polyhedral protoplasmic masses, with intermediate finely branched connective tissue elements, bounding them, and grouping them into nests.

A thin layer of fine nucleated fibres and a few larger blood-vessels seem to separate this structure from the rest of the ovarian stroma (fig. 5), while in time even this boundary will disappear, and the remains of the follicle will no longer be distinguishable as such.

For the sake of comparison I have included here drawings of sections of a "corpus luteum," in an ovary of a *M. rhesus*, in which a six to eight weeks fœtus was present (figs. 10 and 16, Plate 2). It was the only structure of the kind present in either ovary of the animal and is, no doubt, the remains of the follicle from which the ovum was discharged which gave rise to the embryo in the uterus.

This discharged follicle is sunk well within the normal boundary of the ovary and caused no swelling on its surface. The folded walls and central cavity filled with tissue, also the blood-vessels both in the central cavity in the follicle wall and in the surrounding tissue, are all here precisely as in the specimens already described.

The structure of the central tissue (fig. 16) is very similar to that shown in fig. 12, but the tissue of the wall of the follicle is more advanced than in fig. 12, and is intermediate between the latter and the specimen shown in fig. 11.

There is no central blood clot in this specimen.

In conclusion, then, we may describe the changes undergone by the discharged follicle as, firstly, hypertrophy, resulting in a folding of the follicle wall, and a filling up of the central cavity with connective tissue; and secondly, consolidation, which is brought about by the absorption of some of the elements, and the contraction of the other elements, of the tissue concerned.

The increased supply of blood to the wall of the follicle (compare figures 6, 7 and 8), indicates the method whereby the process of absorption is carried out.

Ovulation in Semnopithecus entellus.

I recorded in Part I. of this paper (No. 8), that out of forty-two menstruating specimens of this monkey, none of which had recently borne young, only two had a "recent" discharged follicle in their ovaries. This statement I must now modify.

Sections show that in neither of these cases was a recently discharged follicle present. The vascularity which had misled me was due, not to the presence of a blood clot within the follicles, as I had supposed, but to superficial hæmorrhage in no way connected with recently-discharged follicles.

Thus it is seen, that not a single one of the forty-two menstruating *S. entellus* which were examined, had a recently-discharged follicle in either ovary.

Ovulation in the Human Female.

The work of DALTON (No. 5), so frequently quoted by those who still uphold the view that ovulation and menstruation are coincident, seems to me to fail to prove the view he advanced, primarily because satisfactory proof is not given of the actual rupture of the follicles. The figures given offer no proof whatever of the minute anatomy mentioned in the text, and I know, from the experience I have had while working at the question of ovulation in the rabbit, how difficult it is always to determine satisfactorily whether or not a follicle has been ruptured.

The only corpora lutea which are definitely shown in DALTON'S works to have a ruptured wall, are those drawn in figs. 10 and 11; they were observed in women who died, the first a few hours after delivery at term, the second three days after delivery; these may therefore be disregarded. The figures of so-called corpora lutea supposed to be formed during menstruation, do not definitely show rupture. Fig. 3, nine days after menstruation, and fig. 4, ten days after menstruation, are doubtless intended to show the point of rupture, but they do not at all prove it, while fig. 1, two days after menstruation, shows no sign of rupture, and one would expect the rupture to be more easily seen then than seven or eight days later.

It is not enough to show a prominent follicle full of blood as proof that the follicle has ruptured; it is quite certain that a follicle may rupture without the subsequent formation of a blood clot within it, and it is, in my opinion, equally certain that a blood clot may be present in a degenerate follicle which has not burst and which will not burst; I have many examples of rabbits' ovaries which I think conclusively prove this latter statement.

MARTIN (No. 12) considers that menstruation and ovulation are generally coincident, but either may take place without the other, exceptionally.

CHAZAN (No. 4), after a long critical study of the subject, concludes that the ripening and bursting of Graafian follicles goes on uninterruptedly, and is in no way bound to the time of menstruation; at the same time he holds that the process of menstruation is connected with the scope of ovulation, but the connection is not one of time.

CHAMPNEYS (No. 3) is disinclined to dissociate ovulation and menstruation, and argues that the congestion which affects the uterus also affects the ovaries and the rest of the pelvic organs.

LEOPOLD and MIRONOFF (No. 11), in their recent elaborate study of ovulation in the human female, give the result of their examination of forty-two cases, which comprise examples of almost all stages of the menstrual cycle. From these results they conclude that menstruation and ovulation fall together in thirty of these cases, and that menstruation without ovulation occurs in twelve.

Unfortunately these authors do not give any satisfactory figures of the specimens from which they draw their conclusions, and it is difficult to form an opinion as to the correctness of their interpretation of a recently-ruptured follicle, or of a ripe vesicle ready to burst.

Such statements occur as, for instance, that a certain follicle (seen in an ovary which was excised some days after menstruation) would have ruptured at the next menstrual period. As it is impossible to verify such a statement, and as its enunciation demonstrates a preconceived opinion, one naturally looks with caution upon the conclusions arrived at. The material, which these authors investigated, was most carefully chosen, and was obtained by operation from patients who were able to give satisfactory information of their menstrual history for the previous year.

The part which congestion plays in the matter of ovulation, they claim to be of very great importance. Chronic inflammation of the ovary and surrounding parts is, they say, accompanied by a rapid development and ripening of the ova; while anæmia checks, if it does not entirely prevent, the rupture of follicles. They describe a ripe follicle as thin-walled and characteristically congested with blood, and a typical corpus luteum as being, on the third day after bursting, a large cavity filled with blood; they conclude that the bursting of a follicle demands a strong blood-pressure to the generative organs, and that it is brought about by the swelling influence of menstrual congestion.

On the other hand, they state that, in spite of regular "periods," a follicle does not always rupture, and that a corpus luteum may form when menstruation does not coincide with its formation; they add that large ripe follicles are found in the ovaries at all periods of the menstrual cycle, from the third to the thirtieth day, and they own that these may rupture, and conception may take place, at any time.

Finally, they define menstruation as a period of bleeding from the mucous membrane; they add that the bleeding is connected with the presence of the ovary and with sufficient growth of uterine mucous membrane, and they conclude that, without the mutual action of both these factors, a typical menstrual bleeding does not take place. At the same time they qualify this conclusion with the remark, that uterine bleeding does not depend upon the ripening or bursting of a follicle, and that menstruation is, therefore, due less to the rupture of an ovarian follicle than to the atrophy of uterine mucous membrane.

It is not an easy matter to reconcile these various conclusions. One is forced, it appears to me, to believe that menstruation and ovulation in the human female are governed, either by individual peculiarities, or by two or more laws, which do not operate always at the same time.

The varied conclusions which many eminent investigators have independently arrived at, can only be reconciled with one or other of these assumptions, and the results of LEOPOLD and MIRONOFF's work certainly give increased force to the latter view.

My own researches on monkeys have not been sufficiently complete to enable me to compare what happens in their case, with the story LEOPOLD and MIRONOFF tell. There is good reason to believe that the monkeys which I have investigated have a definite breeding season, and it must be remembered that I have only had an opportunity of examining them at a time which was not the breeding time. I have found that at this period ovulation is exceedingly rare, although menstruation seems to occur regularly enough. It is quite possible that, during the breeding season, ovulation and menstruation may, as a general rule, have some definite close relation the one to the other; at non-breeding times this is certainly not the case.

Such comparison as we are able to make between the two animals, man and monkey, lies in the fact that they both may menstruate without ovulation taking place. The monkey during non-breeding times rarely ovulates, the human female also does not at all times do so; but whether these times in the human species are at regular or irregular intervals, and whether they have any relation to definite times for conception and breeding, there is no present means of knowing. Upon this latter point I have some words to add in the following section.

The Discharged Follicles of Monkeys as Compared with those of the Human Female.

In concluding this account of the discharged follicles of *M. rhesus*, which I have examined, I would especially draw attention to the absence of a blood clot in any of them. **Dalton** (No. 5) describes the normal human corpus luteum as filled with blood soon after rupture has taken place, and he thinks that when no blood clot is present it is probably due to abnormal menstrual conditions.

These views seem to be adopted by a considerable proportion of the medical profession, although some take the opposite view and, like **Coste**, consider the presence of a blood clot in the follicle to be an abnormal condition.

I have no experience myself of the subject, but it would seem to be undoubtedly the fact that, in the human female, discharged follicles sometimes have a blood clot within them and sometimes there is no blood clot present. If the presence of a blood clot in the discharged follicle of the human female is a normal condition, then the discharged follicles of *M. rhesus* described above, differ in a marked manner from them, and yet they are both menstruating animals.

With regard to *M. rhesus* it may be suggested, in the case of the follicle drawn in fig. 8, that it was ruptured when menstruation was not going on, and that as the vessels of the ovary were not congested to the same extent as they would be during the menstrual period, the absence of a blood clot in this follicle may readily be accounted for.

Leopold and **Mironoff** (No. 11) hint at some such difference in the human corpora lutea. But the follicle drawn in fig. 9 was obtained from an animal while undergoing Stage VII. of menstruation, and yet in this case no blood clot is present. A few scattered red blood corpuscles are found near the edge of the follicle (fig. 14), but there is certainly no blood clot. This would seem to show very clearly, first, that ovulation is not caused by the direct presence of free blood in the follicle, as was at one time believed, and secondly, that the congestion of the menstrual period is not the cause of the presence of a blood clot in the discharged follicle.

There is, however, another reason which might account for the absence of a blood clot in these follicles of *M. rhesus*, and it is this, that they were not formed during the breeding season.

I have no experience myself of the relative congestion of the ovaries of monkeys during the breeding and non-breeding seasons, but I have thought it might be quite possible that there is a considerable difference in the amount of blood supplied to the ovaries at these different times, and that, during the breeding season, a blood clot might be formed within the discharged follicle.

I have enquired about this point from Professor HUBRECHT, who with untiring energy has collected a very large series of the generative organs of pregnant monkeys, lemurs, and insectivora, and he has most kindly sent me a brief account of the newly discharged follicle of *Tarsius spectrum.*

In this animal, after the ovum is discharged, the cavity of the follicle contains only an albuminous coagulum; very soon congestion of the walls of the follicle takes place, and at the same time a considerable proliferation of the cells of the wall greatly reduces the size of the central cavity; subsequently, extravasation of blood takes place into the remains of the cavity, and a small blood clot is formed there which persists for a short time only.

Thus it may be said in regard to monkeys that, while in the non-breeding season (*M. rhesus*) the discharged follicle contains no blood clot, during the breeding season (*T. spectrum*) a blood clot is formed therein.

This condition in monkeys becomes of increased interest when compared with the condition in the human female.

In both animals menstruation occurs, in both, ruptured follicles containing a blood clot and ruptured follicles without any blood clot are found.

Now, with regard to monkeys, I have shown that the evidence is opposed to the view that menstruation has anything to do with the presence or absence of a blood clot in the follicle, and I have advanced some evidence infa vour of the view that it is to the presence or absence of the breeding season we must look for an explanation of the difference.

The question naturally arises, whether we may look for a similar explanation of this same variation in the human female. I do not suggest that there is evidence of the occurrence of one or other of these two kinds of discharged follicles at *particular* seasons, but I do suggest there is some reason to believe that the human female is not always in a condition to breed, and that it is during such times that a discharged follicle contains no blood clot.

It is possible to carry this analogy still further, and to suggest, that the occurrence of non-breeding times in the civilised woman of the present day, although it may now be an irregular occurrence, is not incompatible with the belief that at one period of its existence the human species had a special breeding season.

Considered alone, of course, this slender evidence is of little value, but when it is placed side by side with other evidence, of which there is a considerable amount, the deduction is by no means an impossible one.

I had intended here to include a brief account of certain evidence, which I have collected, upon this question of a primitive human breeding season, but I find the subject will be better discussed in a separate paper, and I will content myself with drawing attention to this single point here.

Summary.

Anatomy of the Cervix.—The existence of a valvular structure in the cervix is described. It seems probable that this valve assists in the retention of spermatozoa in the uterus.

Breeding.—The probability of different breeding times for this monkey in different parts of the continent of India is argued, and the existence of a definite breeding season maintained.

It is pointed out that further information is required to establish definitely the period of gestation.

Menstruation.—A regular menstrual flow is described.

External Signs of Menstruation.—A congestion of the skin of the abdomen, legs, and tail, a swelling and congestion of the nipples and vulva, and flushing of the face are prominent signs.

Menstrual Discharge.—This consists of a viscid, stringy, opaque white fluid filled with granules, and containing also red blood corpuscles, pieces of uterine tissue both stroma and epithelium, and also leucocytes.

Leucorrhœa was observed in one case, and consisted of a viscid, opaque fluid filled with granules chiefly derived from the uterus, and squamous epithelial cells from the vagina.

Superficial Menstrual Phenomena.—The stages of menstruation adopted in this paper are identical with those fully described in Part I., on *Semnopithecus entellus.* The smooth surface of the mucosa (Stage I.) becomes swollen, and opaque (Stage II.), then flushed (Stage III.), then highly congested (Stage IV.). Dark red spots, lacunæ, appear on the surface (Stage V.), and free blood in the uterine cavity (Stage VI.). The menstrual clot is formed (Stage VII.), and recuperation follows (Stage VIII.).

Histology of Menstruation.—The account of the histological changes which take place, resolves itself into a repetition of the description given of *S. entellus* in Part I. of this paper. The mucosa of *M. rhesus* is thicker, the protoplasmic network of the stroma denser, and the glands more numerous and more branched than in *S. entellus.*

The increase in number of the nuclei in Stage II., caused by amitotic division and fragmentation, is very marked; hyperplasia occurs, and the mucosa becomes swollen.

The vessels increase in number and size, and leucocytes increase in number in Stage III.

Hypertrophy of the walls of the vessels, followed by degeneration in the superficial part of the mucosa, occurs in Stage IV., and lacunæ are formed in Stage V., while degeneration of the epithelium and superficial stroma, followed by rupture of the lacunæ and free bleeding, is seen during Stage VI.

The denudation of the stroma and the formation of the mucosa menstrualis and clot in Stage VII. is the same as in *S. entellus*, and so also is the recuperation of hypertrophied vessels, the formation of new capillaries, and the reclamation of red blood corpuscles in the stroma during Stage VIII.

With regard to the new uterine epithelium, fresh evidence is found of its formation, partly from stroma tissue, and partly from the epithelium of portions of the uterine glands left *in situ* after denudation has taken place.

Menstruation in Man.—No recent work on human menstruation has been observed which is opposed to the account given for monkeys, while MINOT'S work gives additional reason for believing that the process in these two animals is practically identical.

The Re-formation of Uterine Epithelium from Stroma Tissue.—The opinion herein urged on this matter is also held by DUVAL and JOHNSTONE, while it is opposed by KIERSNOWSKI, STRAHL, and NOLL. It appears, however, that while the three latter observers satisfactorily show a re-formation of some uterine epithelium, by direct growth, from existing epithelial elements, yet they do not show any sufficient reason for their denial of the observations of DUVAL, while one of the figures given by KIERSNOWSKI indicates that he has probably wrongly interpreted his specimens.

DUVAL, on the other hand, only arrived at the view he now holds after examination of a large number of preparations, and he has no doubt whatever of its truth.

Ovulation in M. rhesus.—Confirmation is given of the opinions before advanced (Part I.), viz., that ovulation does not necessarily occur during each menstrual period, that it is not necessarily brought about by menstruation, and that the ripening of an ovum in the ovary may be a process independent of the process of menstruation.

In only one out of seventeen cases of menstruating *M. rhesus*, can it possibly be urged that ovulation and menstruation were coincident.

An account is given of a series of discharged follicles, and the histological changes undergone by these structures is traced, until at last they are merged into the normal ovarian stroma.

The absence of a blood clot in any of the discharged follicles is drawn attention to, and the history of the connective tissue which occupies the cavity of these follicles, is followed. The folding of the wall of the follicle and the transformation of its cells into ovarian stroma tissue are also given.

Ovulation in S. entellus.—An error made in Part I. is now corrected, and it is shown that not a single specimen, of the forty-two menstruating *S. entellus* which were examined, had a recently-discharged follicle in either ovary.

Ovulation in the Human Female.—It is pointed out, that it is not enough to show a prominent follicle filled with blood as proof that the follicle has been ruptured. It is certain that a follicle may rupture without the formation of a blood clot (man and monkey), and it is equally certain a blood clot may be present in a degenerate follicle which has not, and which never will, rupture (rabbit). It is also shown that it is not possible to diagnose the date at which a particular follicle will rupture. Although ovulation and menstruation may be coincident, this is certainly not always the case (man and monkey), and one is forced to believe that these two processes are governed by two or more laws, which do not always operate at the same time.

The discharged Follicles of M. rhesus *compared with those of the Human Female.* Attention is drawn to the fact that, in the human female, some discharged follicles contain a blood clot, whereas some do not.

In monkeys, during the non-breeding season (*M. rhesus*) no blood clot is present in newly-discharged follicles, while in the breeding season (*T. spectrum*) a blood clot is present in them. It is shown that the presence of a blood clot in monkeys is not due to the coincidence of ovulation with menstruation, and it is suggested, on the other hand, that its presence is due to the coincidence of ovulation with the breeding season. A further suggestion is then made, that the presence or absence of the blood clot in the discharged follicles of the human female, is due to the coincidence of ovulation with a favourable time for conception. It is pointed out that women are not always in a condition to breed, and that it is possible the occurrence of periods during which they do not conceive, may justly be compared with the non-breeding times of monkeys.

POSTSCRIPT.

February 17, 1897.

Since the above was written, a paper by **WESTPHALEN** (No. 18) has appeared. His material was obtained by curetting or from uteri amputated for chronic metritis, and did not include a complete series.

He describes the dilatation of blood-vessels before menstruation begins, the infiltration of blood in the upper part of the mucosa, and the beginning of the formation of lacunæ.

Here his observations stop until after menstruation is over, when he finds some evidence of the shedding of uterine epithelium, but does not, of course, see evidence at that stage of the discarding of stroma tissue; he does not appear to have examined the menstrual discharge to see what is thrown off, and concludes that the superficial tissue, which was raised by the formation of the lacunæ, for the most part sinks down again when the lacunæ rupture, and is rapidly covered by epithelium.

After menstruation is over, according to this author, regeneration takes place, and this process lasts until about the eighteenth or nineteenth day. During this time karyokinesis was observed in each of the structures composing the uterine mucous membrane, at first only here and there, but from the sixth to the eighteenth day in great profusion; and he points out that he saw no sign of amitotic division.

After the eighteenth day a pre-menstrual swelling of the mucosa is described; it begins gradually, and consists of a serous saturation of the stroma, and an increase in volume of the glands.

If this account be correct, there is a very considerable difference between the phenomena attending menstruation in monkeys and in the human female.

The preliminary stages of congestion of the mucosa, and the formation of lacunæ, in the woman, **WESTPHALEN** says, are similar to what I have described for the monkey; and as he did not observe the stage during which the lacunæ are ruptured, it is possible to account for the variation in our respective views regarding the amount of uterine tissue which is discarded at that time.

But his description of the regenerative process and of the pre-menstrual swelling is entirely at variance with my observations.

The regenerative process in monkeys consists of a *shrinkage* of the bulk of the mucosa, a return of extravasated blood to the circulatory system, and a re-formation of the uterine epithelium; while, in the human female, it would appear that profuse karyokinesis takes place during that time, and that there is an *increase* of mucosa tissue.

Again, the pre-menstrual swelling in monkeys is accompanied by a very rapid increase, in numbers, of the nuclei of the stroma tissue, by, in my opinion, amitotic division; while in the human female there is no multiplication of nuclei, and the swelling is due to serous saturation of the stroma. Thus the increase in numbers of the nuclei of the stroma, in the human uterus, occurs in the inter-menstrual period, it occupies a considerable length of time, it is a leisurely process, and it is brought about by karyokinesis; while the same process in the monkey's uterus occurs immediately before congestion begins, it is a very rapid process, and is brought about by amitotic division, and by fragmentation of the nuclei.

I have suggested in my former paper that the absence of the phenomena of karyokinesis in these dividing nuclei may be due to their minute size, and to the meagre quantity of protoplasm surrounding them; it is possible, also that the rapidity of their increase may also have some bearing on their method of division.

In this connection it is interesting to notice that **BALBIANI** and **HENNEGUY** (No. 1A) have shown that, under certain circumstances, the ends of the tails of two tadpoles, placed in contact, will, in an hour and a half, grow together by means of the superficial growth of their epithelial cells, and that this very rapid growth is brought about by amitotic division.

STRASSMANN (No. 16A) has attempted to show that menstruation and "heat" are brought about by the increase of inter-ovarian pressure; that the pressure exerted by the growing Graafian follicle on the sensory nerve-endings in the ovary is the exciting cause of the reflex action, which brings about congestion of the genital organs, menstruation, or "heat."

Whilst this theory is not opposed to the fact that menstruation and ovulation are quite distinct processes, since it does not presuppose that the Graafian follicle necessarily ruptures, still it is in direct opposition to the fact that menstruation may occur after ovariotomy has been performed, and I do not find that STRASSMANN has satisfactorily disposed of this objection to his theory.

Finally, I would draw attention to the fact that SOBOTTA, in his admirable work on the corpus luteum of the mouse (No. 14A), lays great stress upon the fact that the increase in size of the wall of the newly-discharged follicle is due to the hypertrophy of its cells, and not to the increase in number of those cells. This result is in accord with the view I have independently arrived at, regarding the increase in size of the wall of the newly-discharged follicles of *M. rhesus*, and has not been, as far as I am aware, drawn attention to elsewhere.

LIST OF PAPERS REFERRED TO.

No. 1. BALBIANI et HENNEGUY. Comptes Rendus, vol. 123, 1896.

" 1A. BLANDFORD. The Fauna of British India, Part I., Mammalia. 1888.

" 2. BRESCHET. Recherches anatomiques et physiologiques sur la gestation des Quadrumanes. Mémoires de l'Académie des Sciences, vol. 19.

" 3. CHAMPNEYS. On Painful Menstruation. The Harveian Lectures for 1890 (1891).

" 4. CHAZAN. Ovulation und Menstruation. Archiv für Gynäkologie, vol. 36, 1889.

" 5. DALTON. Report on the Corpus Luteum. Transactions of the American Gynæcological Society, vol. 2, 1878.

" 6. DUVAL. De la régénération de l'épithélium des cornes utérines après la parturition. Comptes Rendus et Mémoires de la Société de Biologie, Series ix., vol. 2, Dec. 13, 1890.

" 7. GEOFFROY SAINT-HILAIRE et CUVIER. Hist. Natur. des Mammifères.

" 8. HEAPE. The Menstruation of *Semnopithecus entellus*. Philosophical Transactions of the Royal Society, vol. 185, 1894.

" 9. JOHNSTONE. Menstruation, its Necessity and Purpose. American Journal of Obstetrics, vol. 24, 1891.

" 10. KIERSNOWSKI. Zur Regeneration des Uterus-Epithels nach der Geburt. MERKEL und BONNET, Anatomie und Entwickelungsgeschichte, vol. 4, Part iii., 1894.

No. 11. Leopold und Mironoff. Beitrag zur Lehre von der Menstruation und Ovulation. Archiv für Gynäkologie, vol. 45, 1894.

„ 12. Martin. The Physiology and Histology of Ovulation, Menstruation, and Fertilization, &c. Hirst's System of Obstetrics, vol. 1, 1888.

„ 13. Minot. Text Book of Human Embryology, 1892.

„ 14. Noll. Beiträge zur Kenntniss des Raubtier-Uterus nach dem Wurf. Merkel und Bonnet, Anatomie und Entwickelungsgeschichte, vol. 5, Part xvi., 1895.

„ 14a. Sobotta. Ueber die Bildung des Corpus luteum bei der Maus. Archiv. f. Mik. Anat,, vol. 47, 1896.

„ 15. Strahl. Die Regeneration der Uterus-Schleimhaut der Hündin nach dem Wurf. Anat. Anzeiger, vol. 9, No. 21.

„ 16. —— Die puerperale Uterus der Hündin. Merkel und Bonnet, Anatomie und Entwickelungsgeschichte, vol. 5, Part xvi., 1895.

„ 16a. Strassmann. Beitrag zur Lehre von der Ovulation, Menstruation, und Conception. Arch. f. Gnaekologie, vol. 52, 1896.

„ 17. Sutton. Menstruation in Monkeys. British Gynæcological Journal, vol. 2, 1880.

„ 18. Westphalen. Zur Physiologie dur Menstruation. Arch. f. Gynaekologie, vol. 52, 1896.

Description of Plates 1 and 2.

Reference Letters.

bl.c.	red blood corpuscles.	*gr.v.*	Graafian vesicle.
bl.v.	blood vessel.	*in.os.*	internal os.
c.	cervix.	*lac.*	lacuna.
c.c.	canal of cervix.	*muc.*	mucosa.
cav.tis.	tissue within the cavity of the follicle.	*o.*	ovary.
		ut.	uterus.
ep.	epithelium.	*ut.c.*	cavity of the uterus.
ex.os.	external os.	*vag.*	vagina.
f.w.	wall of the follicle.	*vl.*	valve.

PLATE 1.

Fig. 1. Stroma cells dividing into two. (Reichert's Imm. $\frac{1}{15}$ occ. 4.)

Fig. 2. Showing division by fragmentation of the nuclei of the stroma. *a, b,* and *c,* groups of nuclei derived from a single nucleus by fragmentation. Reichert's Imm. $\frac{1}{15}$ occ. 4.)

Fig. 3. The uterus, cervix, and part of the vagina of *M. rhesus.* It is cut open along the left and anterior borders of the organ, and the walls of the enclosed cavity are exposed. The uterine mucosa is smooth and soft. The canal of the cervix is longitudinally folded, and from the ventral wall of the cervix a thick lobe projects, which fits between two lobes on the dorsal wall and forms therewith a valve. (× 1½ times.)

Fig. 4. Longitudinal vertical section through the antero-posterior walls of the uterus, cervix, and part of the vagina of *M. rhesus.* The cavities of the uterus and vagina, and the long narrow tortuous canal of the cervix are shown. The valve-like structure is also shown *in situ,* the single lobe of the anterior wall of the cervix being fitted between the two lobes on the posterior wall.

Fig. 5. Remains of a ruptured follicle, from the ovary of a *M. rhesus* undergoing Stage V. of menstruation. The walls of the follicle are no longer folded, and the central cavity is obliterated. (Zeiss, *a**, occ. 2.)

Fig. 6. A ruptured follicle, from the ovary of a *M. rhesus* undergoing Stage IV. of menstruation. The walls are much folded, and hardly distinguishable from the central cavity. Four Graafian vesicles lie outside this follicle. (Zeiss, *a**, occ. 2.)

Fig. 7. A ruptured follicle, from the ovary of a *M. rhesus* which had probably aborted her young. The walls are much folded, and the central cavity, though small, is distinct. (Zeiss, *a**, occ. 2.)

Fig. 8. A ruptured follicle from the ovary of a non-menstruating *M. rhesus.* The walls are but slightly folded, and the contained cavity is wide and large. (Zeiss, *a**, occ. 2.)

Fig. 9. A recently ruptured follicle, from the ovary of a *M. rhesus* undergoing Stage VII. of menstruation. The walls are not folded, the follicular cavity is large and pear-shaped, the apex approaching near to the surface of the ovary, which, at the point *x*, is devoid of epithelial covering. (Zeiss, *a**, occ. 2.)

PLATE 2.

Fig. 10. A corpus luteum from the ovary of a *M. rhesus,* in which a six to eight weeks old embryo was found. The follicle has sunk away from the ovarian epithelium, the walls of the follicle are much folded, and the contained cavity is small and narrow. (Zeiss, *a**, occ. 2.)

Fig. 11. A piece of the follicle represented in fig. 5, showing the nests of polyhedral cells, or of nuclei in a polyhedral mass of protoplasm, and surrounded by branched connective tissue elements. (Zeiss, C, occ. 4.)

[illegible] represented in fig. [illegible] showing the minute branched [illegible] cavity of the follicle, the [illegible] are also shown. (Zeiss, C, oc. 4.)

[illegible] represented in fig. [illegible] the tissue in the cavity of the [illegible] connective tissue, continuous with the [illegible] (Zeiss, C, oc. 4.)

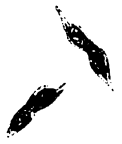
[illegible] represented in fig. [illegible]. The material in the cavity [illegible] it consists of a network of finely granulated [illegible] few red blood corpuscles lie within its meshes near the wall [illegible]

The [illegible] of the follicle is formed of branching cells, except along its internal edge, and here it is composed of longitudinal, finely drawn out [illegible] sharply marked off from the follicular cavity, but continuous with the branched processes of the deeper seated cells of the wall. (Zeiss, C, [illegible])

[illegible] of the apex of the follicle drawn in fig. 9, together with the tissue intervening between it and the surface of the ovary. The ovarian epithelium is absent at the point x, and is much flattened on either side of this point. Between the apex of the follicle and the point x the tissue [illegible] and open; it consists of a wide-meshed connective tissue with few nuclei, and many extravasated red-blood corpuscles are scattered [illegible] (Zeiss, A, oc. 4.)

[illegible] of the follicle represented in fig. 10, showing the branched nuclei of the tissue contained within the follicle, and the early formation, in the [illegible] wall of nests of nuclei surrounded by branched connective tissue [illegible] (Zeiss, [illegible], oc. 4.)

Fig. 1.



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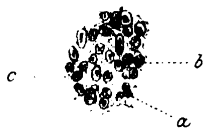

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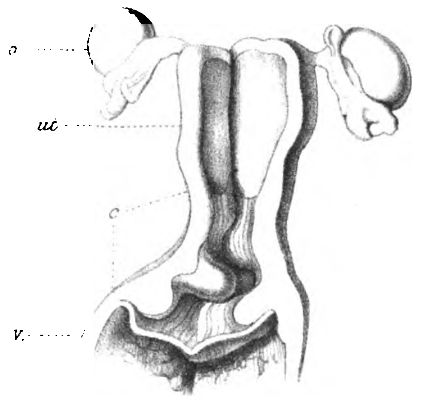

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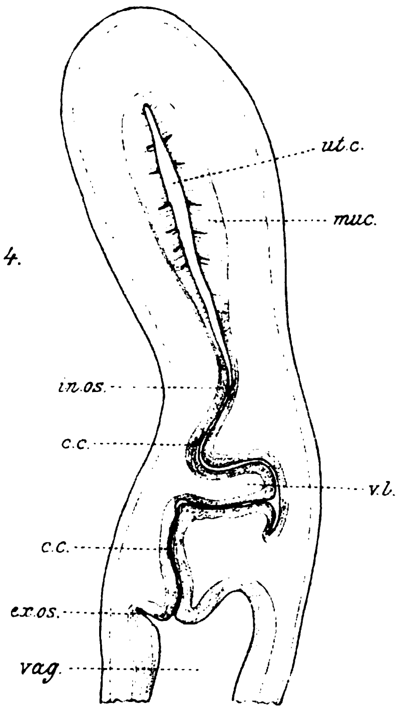

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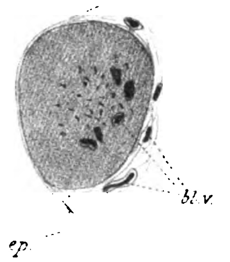

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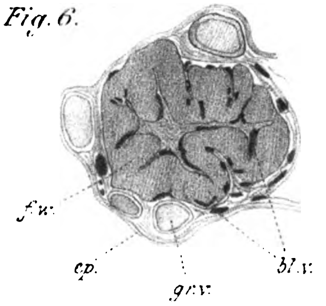

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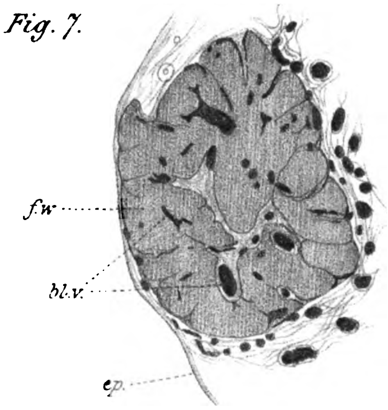

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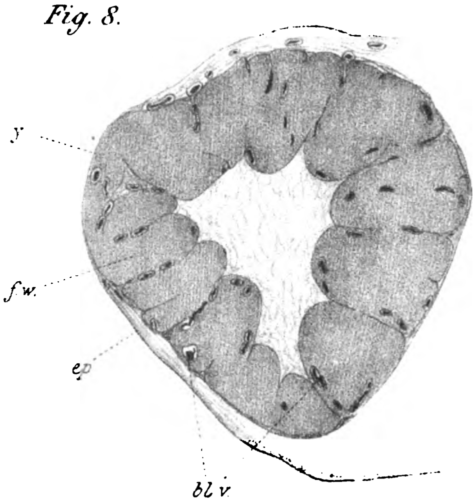

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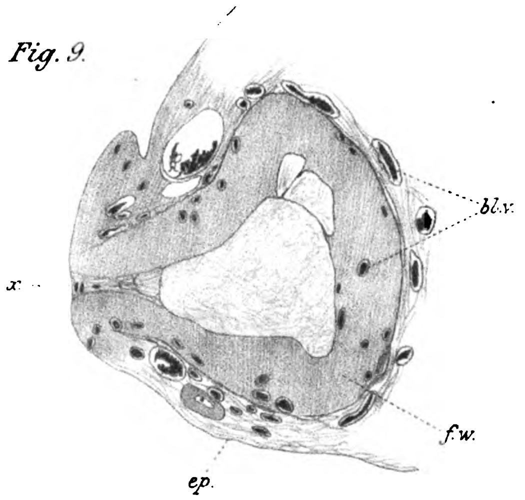

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Fig. 12. A piece of the follicle represented in fig. 7, showing the minute branched nuclei embedded in a matrix, which fills the cavity of the follicle, the branched cells of the follicle wall are also shown. (Zeiss, C, occ. 4.)

Fig 13. A piece of the follicle represented in fig. 8; the tissue in the cavity of the follicle is a very loose, wide-meshed connective tissue, continuous with the branched cells of the follicle wall. (Zeiss, C, occ. 4.)

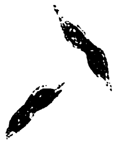
Fig. 14. A piece of the follicle wall represented in fig. 9. The material in the cavity of this follicle is not cellular, but consists of a network of finely granulated material. A few red blood corpuscles lie within its meshes near the wall of the follicle, but there is no blood clot.

The wall of the follicle is formed of branching cells, except along its internal edge, and here it is composed of longitudinal, finely drawn out cells, sharply marked off from the follicular cavity, but continuous with the branched processes of the deeper seated cells of the wall. (Zeiss, C, occ. 4.)

Fig. 15. A piece of the apex of the follicle drawn in fig. 9, together with the tissue intervening between it and the surface of the ovary. The ovarian epithelium is absent at the point *x*, and is much flattened on either side of this point. Between the apex of the follicle and the point *x* the tissue is loose and open; it consists of a wide-meshed connective tissue with few nuclei, and many extravasated red-blood corpuscles are scattered about therein. (Zeiss, A, occ. 4.)

Fig. 16. A piece of the follicle represented in fig. 10, showing the branched nuclei of the tissue contained within the follicle, and the early formation, in the follicle wall, of nests of nuclei surrounded by branched connective tissue cells. (Zeiss, C, occ. 4.)

Fig. 1.



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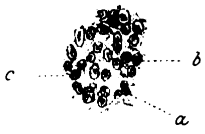

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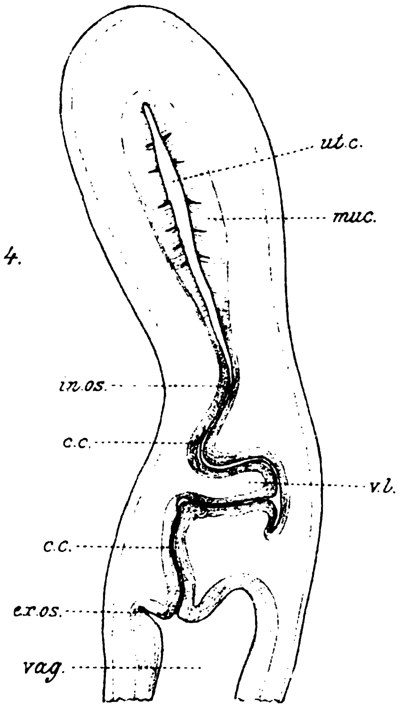

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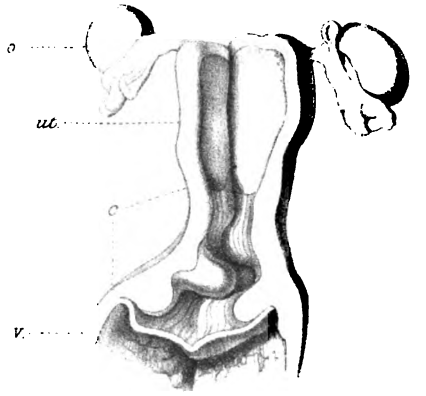

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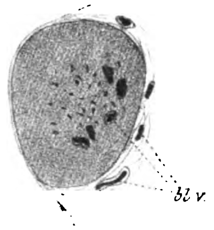

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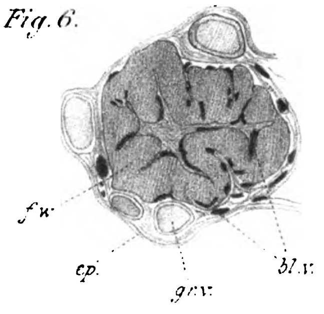

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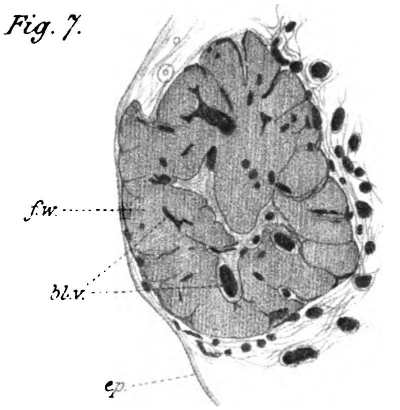

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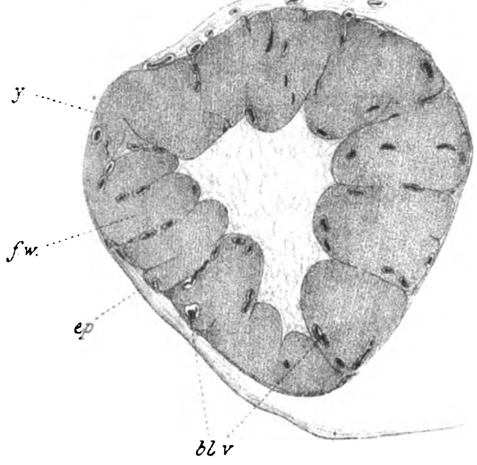

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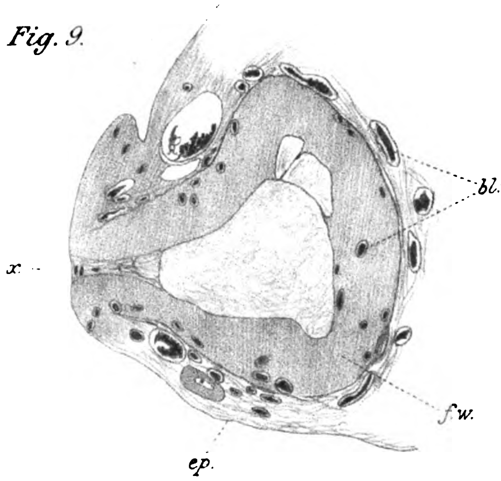

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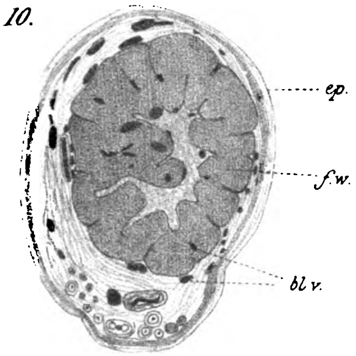
Fig. 10.



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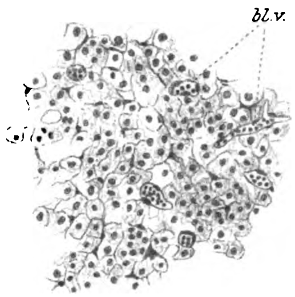

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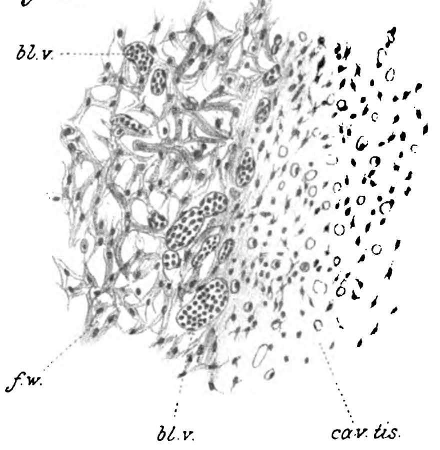


Fig. 13.

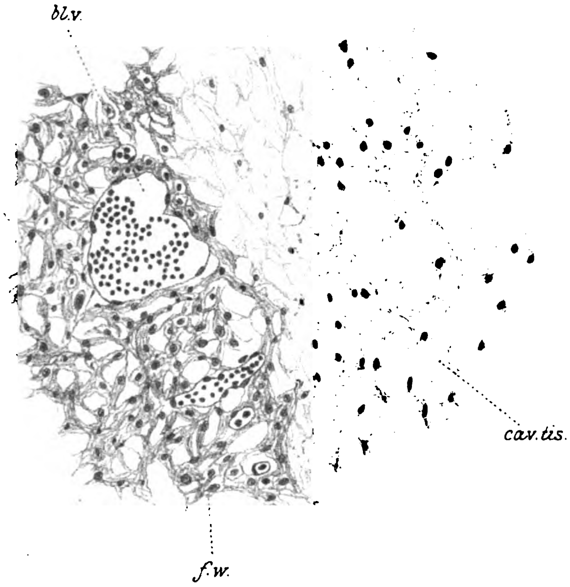


Fig. 14.

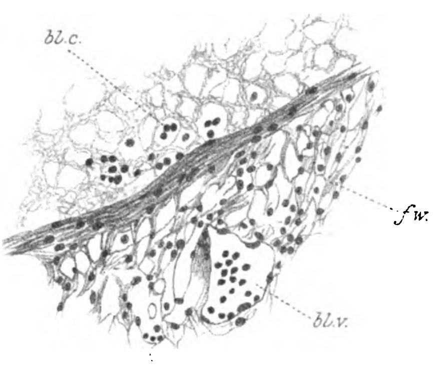


Fig. 15.

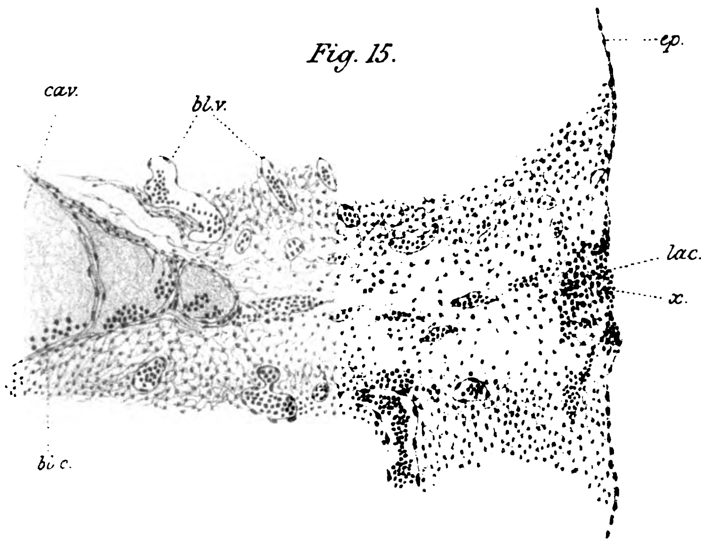
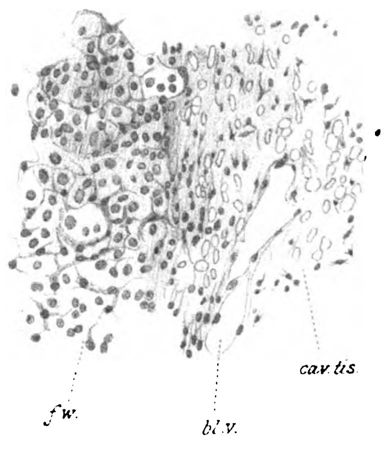


Fig. 16.



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IV. *On the Action of Light on Diastase, and its Biological Significance.*

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In the course of a series of investigations into the chemistry and physiology of foliage leaves, made some years ago by Messrs. Brown and Morris,* among other discoveries of interest, those observers ascertained that the quantity of diastase that the leaves of many different species of plants can be shown to contain, varies considerably during a day of twenty-four hours. It is at its maximum in leaves gathered in the early morning, and at its minimum after a period of exposure to light, as in leaves gathered at 5 p.m. Those observers put forward two hypotheses to explain this phenomenon. The first is that during the day, particularly when the sun is shining, the diastase is used up gradually in dissolving a portion of the starch as it is formed in the chloroplasts, such portion being converted into sugar to meet the immediate needs of the cell protoplasm. This theory involves the acceptance of the view that the starch of the chloroplasts is the final product of the assimilation of the CO_2 absorbed and that its manufacture is altogether an "upgrade" process. Their experiments, however, led them to contest this assumption, and to put forward in contradistinction to it the theory that starch is, in the chloroplasts as elsewhere, always a reserve product, and that its appearance indicates that more carbohydrate is being formed than can be at once either used by the protoplasm or removed from the cell, the surplus being temporarily deposited by the protoplasm as starch. On this view the needs of the cell do not call for the conversion of starch into sugar, but are supplied from the sugar, which all botanists agree is antecedent to starch. They therefore reject this hypothesis, in the light of the experiments referred to, which are detailed in their memoir.

Their second hypothesis, which they regard as a more probable one, is that the formation or secretion of diastase is irregular, being a starvation phenomenon, none of the enzyme being formed until the needs of the cell demand the transformation of the stored starch, either for immediate consumption in the cell, or for removal to a more permanent reservoir.

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* "A Contribution to the Chemistry and Physiology of Foliage Leaves," 'Journ. Chem. Soc.,' May, 1893.

There is a good deal to be said for this view; indeed the authors give some cogent evidence in support of their hypothesis. If we admit, however, that it is probably sound, it is insufficient to explain all the facts, for it gives no reason for the actual diminution of the diastase which can be observed after a subsequent period of illumination.

From the observations of MARSHALL WARD* and other observers who have studied the effect of light upon the living substance of many micro-organisms, it seems at least possible that the light to which the leaves are exposed during the daytime may have a destructive effect upon the enzyme, as it has upon the life of the bacteria and other lowly forms that have been investigated. This hypothesis need not, of course, vitiate the conclusions of BROWN and MORRIS, that diastase is secreted under the conditions they suggest; it rather supplements than contravenes them.

Some time after the appearance of BROWN and MORRIS's memoir, the author undertook a series of experiments to test the validity of the supposition just put forward. These have now extended over a period of three years, and have led to certain conclusions as to the effect of light in general, and of the different regions of the spectrum in particular, upon the secretion and destruction of diastase, which, perhaps, throw some light upon other problems connected with the nutrition of the vegetable organism.

Method of Experiment.

In carrying out these investigations various preparations of diastase were used. They comprised extract of malt, extract of foliage leaves (usually those of *Phaseolus vulgaris*), and diluted human saliva. To prepare the malt diastase, some ground malt was usually steeped in water for several hours and the mixture filtered. Alcohol was added to the filtrate till it contained about 30 per cent., when a flocculent precipitate fell. This was separated by filtration and dissolved in a feebly antiseptic solution, containing ·2 per cent. of potassic cyanide. In a few experiments the malt extract was used without the precipitation by alcohol, but the presence of sugar and colouring matter involved difficulties in the subsequent treatment. Experiments showed that 30 per cent. of alcohol caused the greater part of the diastase to be thrown down. The solution, however, always contained a little proteid matter.

The extract of the Phaseolus leaves was prepared by grinding the leaves, either fresh gathered, or after drying them in an air bath at 35° C., into a paste in a mortar and extracting them for several hours in water, the same proportion of KCN being added as an antiseptic. They were then filtered and the extract used without further treatment. It was usually faintly tinged with green and contained a little proteid matter. When examined by the spectroscope it gave an absorption spectrum which will be described in a subsequent section of this paper. In a few cases the leaves before being dried were killed by exposure to the vapour of chloroform.

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* "On the Action of Light on Bacteria," 'Phil. Trans.,' vol. 185, B, pp. 961–986, 1895. (Other papers are quoted in Professor WARD's Memoir.)

To prepare the salivary diastase, freshly-secreted saliva was diluted by the addition of about an equal bulk of water and the mucin was precipitated by a trace of acetic acid. It was then filtered and carefully neutralised by either dilute ammonia or crystals of potassium bicarbonate. The same antiseptic was added as in the other cases, ·2 per cent. being the quantity always present. The solution so prepared was faintly opalescent and contained a trace of proteïd matter.

The diastasic extracts so prepared were found to keep extremely well, many preparations being quite unchanged after six months. The antiseptic used was found to be quite without effect upon the enzyme.

The extracts were exposed in different media to the action of the light for several hours; simultaneously further quantities were placed in exactly similar conditions to the exposed ones, except that they were protected in various ways from any illumination. Each experiment was thus carefully controlled, and every precaution was taken that the further results might be strictly comparable.

The source of illumination was in some cases sunlight, either that of a bright sun, or of the light reflected from a blue sky or light clouds. In some cases a dimmer light was employed, such as is reflected from the denser clouds of a wintry sky. A large number of observations were made by the use of the electric arc. Through the kindness of Mr. BARKER, the Manager of the Electric Light Works, at Cambridge, the author had access to a naked arc lamp, of about 2000 candle power, which was made to play upon the extracts at a distance of about two feet.

During the exposures the temperature which was reached was ascertained by the use of a maximum thermometer. When the electric light was used, this rarely exceeded 27° or 28° C. When sunlight was employed and glass vessels used for the extracts, the illuminated and shielded vessels were exposed side by side in a beaker of water, so that the temperature of both should be the same.

The effect of an exposure for the usual duration of the illumination to a temperature of 27° C. was ascertained separately, and found to be but slight. It was taken into account, where necessary, in comparing the results of different experiments.

In some of the experiments, glass vessels were used to contain the extracts during illumination. These were, at first, tubes, but as the shape of the tube seemed likely to introduce an error, these were abandoned in favour of small flat-sided glass bottles, made to contain about 20 cub. centims. of fluid. The thickness of the liquid in these was about 5 millims.

As glass, however, has been shown by many observers* to be opaque to the ultra-violet rays, when these rays were under observation ebonite cells were employed, the faces of which were covered by quartz plates, cemented to the ebonite by gold size. Some comparative experiments on the effect of glass and quartz as the covering of the cells, were detailed by the author at the meeting of the British Association at Oxford in 1894.*

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* WARD, *op. cit.*

In a few experiments the diastasic solutions were mixed with agar-agar, at a temperature at which the agar-agar was on the point of gelatinisation, and the mixture poured over a flat glass dish, on which it almost immediately formed a film a few millimetres in thickness. The uncovered side was then illuminated.

After the exposure, equal volumes of the exposed and unexposed extracts were mixed with a preparation of starch and digested either at the laboratory temperature, or in an incubator at about 38° C. When the hydrolysis was fairly advanced, both digestions were boiled simultaneously and the products of hydrolysis ascertained by titration with FEHLING'S fluid. In the earlier experiments a weak starch paste (1 per cent.) was employed, but this was afterwards abandoned in favour of a 1 per cent. solution of soluble starch prepared by LINTNER'S method. Some dry potato starch was mixed with hydrochloric acid of 12 per cent. strength, and left in contact with the acid for some days. It was then strained off and dialysed in running water till all traces of the acid had disappeared. The starch was then readily soluble in boiling water, giving a solution which was but slightly opalescent and which filtered rapidly. The solution gave but a faint trace of cuprous oxide when boiled with FEHLING'S fluid, and became pure blue in colour when a little iodine was added to it.

The results of such a digestion, when expressed in terms of the weight of cupric oxide found on combustion, have been ascertained by KJELDAHL† to be proportional to the quantity of enzyme present, if the starch transformation is not allowed to fall below a cupric-reducing power of K 25–30 for the mixed products of hydrolysis.

The titration of the result of each experiment was performed by making the volume up to 100 cub. centims. with water, and boiling it with an excess of FEHLING'S fluid for fifteen minutes. It was then rapidly filtered, and the filter washed several times with boiling water. The filter paper with the cuprous oxide was then dried and burned in a platinum crucible till the oxide was all converted to the cupric condition, and the weight ascertained to the fourth place of decimals. With the comparatively small quantities of oxide present, this method was found to give accurate results.

In all cases where the extract contained sugar, as when fresh malt or leaf extract was used, a separate determination was made of the reduction caused by the volume of the extract, which was deducted from the results in the digestions under examination.

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* 'Annals of Botany,' September, 1894.

† KJELDAHL, 'Résumé du Compte Rendu du Laboratoire de Carlsberg,' 1, 1879.

The Effect Produced by Exposure to all the Rays of the Spectrum.

As glass has been shown to be opaque to the ultra-violet rays of the electric light, it was necessary to expose the extract to the illumination without its interference. The first experiments were performed by mixing a diastasic solution with a little agar-agar, and supporting a film so prepared upon a shallow glass dish.

A quantity of malt was ground and extracted for several hours with a ·2 per cent. solution of potassium cyanide. It was then filtered and yielded a yellowish solution. Alcohol was added till about 30 per cent. was present, when a white precipitate fell. This was rapidly filtered off, drained, and dissolved in the same antiseptic liquid. A quantity of agar-agar solution, containing 3 per cent. of the jelly, was prepared, and just before it was cool enough to gelatinise, a quantity of the diastasic solution was stirred into it. Half of it was then poured into each of two Petri dishes, forming a film of about 3 millims. thickness, and the two allowed to cool. One of these was exposed for 10 to 12 hours to the naked light of the electric arc at a distance of about 2 feet. The lamp was of about 2000 candle-power. After removal, the agar-agar, which had become partially dried, was swelled up again by the addition of sufficient water. The two films, labelled L and D, were then detached from their supports and mixed carefully with 25 cub. centims. of 1 per cent. starch paste, care being taken to make the incorporation of the jelly with the paste as complete as possible. They were then digested in an incubator at 38° C. for 20 hours, the progress of hydrolysis being tested from time to time by adding iodine to a drop or two upon a porcelain slab. The exposed film was much less active than the non-exposed one. When the iodine showed the digestion to be well advanced, the two vessels were removed and simultaneously heated to 100° C., and the sugar titrated as described above.

The resulting weights of cupric oxide were D ·105 grm., L ·028 grm., showing a destruction of diastase in the proportion of about 78 per cent.

Other experiments with agar-agar were less satisfactory, owing to the difficulties of manipulation, and, instead of continuing the use of this medium, it was found better to expose the extracts to illumination in quartz-fronted cells. The first experiment under these conditions was performed with some of the same extract used in the one detailed above, when it was mixed with the agar-agar. The extract was placed in an ebonite cell, the face of which was covered by a quartz plate, about 3 millims. in thickness, which was cemented on by gold size. The cell was placed at the same distance from the lamp as the agar film had been, and remained there for 10 to 12 hours.

5 cub. centims. of this exposed extract was then added to 24 cub. centims. of 1 per cent. starch paste, and a similar quantity of the extract that had not been illuminated was added to a further 24 cub. centims. of the same. They were labelled L and D, and digested for 2½ hours in an incubator at 38° C. The action

was more rapid than when the agar films were used, but the same difference in power was speedily apparent. On titration the weights of cupric oxide yielded were D ·012 grm., L ·005 grm., or about 58 per cent. of the diastase had been destroyed.

These results were repeatedly confirmed, using extracts of various strengths, and varying the times of exposure and the conditions of the subsequent digestions. Under the conditions of exposure quoted, however, the experiments agreed in showing a considerable destruction of the diastase of malt when exposed to the total rays of the spectrum.

Further experiments were then undertaken, using saliva instead of malt extract. It would be tedious to give details of all; a typical one may therefore be selected.

Two cells, with quartz fronts, were taken, and the outer face of one covered over with blackened paper, impervious to light. In each, 15 cub. centims. of saliva, prepared as described above, were exposed to the electric arc for 12 to 14 hours. After removal, 5 cub. centims. of each were mixed with 20 cub. centims. of the same starch paste and digested in the incubator at 40° C. On titration the weights of cupric oxide were D ·0658 grm., L ·0328 grm., so that a little more than half the ptyalin had been destroyed.

A similar result was arrived at with the diastase that can be extracted from foliage leaves. Some leaves of *Phaseolus vulgaris* were made into a pulp in a mortar and extracted with ·2 per cent. potassic cyanide solution. The solution when filtered was pale yellowish-green, but its spectrum showed no absorption bands, except a very faint narrow one at 680 to 690 $\mu\mu$. It cut off the red up to 720 $\mu\mu$, and the blue beyond 480 $\mu\mu$. Exposed for 9½ hours to the electric arc, digested side by side with an unexposed control, and the digestion titrated, the weights of cupric oxide were L ·17 grm., D ·185 grm., a loss of diastase amounting to about 8 per cent.

The effect of the total rays of the spectrum, when allowed to act upon diastase, whether of animal or vegetable origin, is, therefore, destructive, the destruction varying however in amount under different conditions of exposure. The destruction further is progressive, the impairment of diastasic power continuing after removal from the light. An experiment bearing on this point is subjoined :—

Some solution of malt diastase, prepared as in the experiments already described, was exposed to the electric arc in a quartz-fronted cell for 10 to 11 hours, while a control was kept in darkness. 5 cub. centims. of each were then mixed with 25 cub. centims. of 1 per cent. starch paste and digested as usual. On titration the amounts of cupric oxide yielded were D ·085 grm., L ·036 grm., showing a destruction of 42 per cent. of the enzyme. The remainder of each was then set aside for six weeks, when another digestion experiment, in all respects the same as the first, was conducted with them. The final weights of cupric oxide were D ·089 grm., L ·001 grm., showing that the destructive action had gone on until almost all the diastase had disappeared.

The Effect of Light on Extracts Contained in Glass Vessels.

A series of experiments was next undertaken with the view of ascertaining in what part of the spectrum the deleterious rays are situated. The experiments of **MARSHALL WARD** on the influence of light on bacteria have shown that, so far as the latter organisms are concerned, the destructive effect was confined to the blue, violet, and ultra-violet rays, all the red end and the infra-red rays being harmless to them. As already pointed out, glass has been shown to be opaque to the ultra-violet rays, or at least to the ultra-violet of the spectrum of the electric arc. By the use of glass vessels, therefore, the effect of the rays of the visible spectrum and of the infra-red can be examined.

Experiments made with the electric arc, using a solution of precipitated malt diastase, gave a striking result. Two of these, which differed in the conditions of exposure, are detailed below.

20 cub. centims. of the diastasic solution were exposed in a glass cell to a lamp of about 500 candle power for 3 hours. 10 cub. centims. of this and 10 cub. centims. of an unexposed quantity of the same extract were then digested for 4 hours with 25 cub. centims. of starch paste. After titration the weights of cupric oxide were L ·0325 grm., D ·029 grm., or an increase of diastase amounting to 12 per cent.

In the second experiment the exposure was made for 20 hours to the larger arc light, of about 2000 candle power. 12 cub. centims. of the exposed and 12 cub. centims. of the unexposed solution were digested, each with 25 cub. centims. of 1 per cent. starch paste, at 39° C. for 3¼ hours. After titration the weights of cupric oxide were L ·04 grm., D ·03 grm., an increase of diastase amounting to 33 per cent.

As this investigation was undertaken at the outset to ascertain the effect of sunlight on the diastase of the leaf, some experiments may be recorded here in which varying intensities of sunlight were studied instead of the light of the electric arc. Several of these gave instructive results.

Three tubes containing a solution of malt diastase were taken; one, A, was placed in sunshine in the laboratory window; one, B, in diffused light in another window to which the sun had not access; and a third, C, was kept in darkness, the temperatures being kept equal by standing them in beakers of water. After 24 hours, during which there had been about 4 hours bright sunlight, they were examined in the usual way. After titration the weights of cupric oxide were A ·0845 grm., B ·0875 grm., C ·0845 grm. The exposure to bright sun had been without effect, while the effect of the diffused light had been to very slightly increase the diastase.

Another experiment, carried out under the same conditions, except that no observation was made on diffused light, showed that after an exposure of two days, during which there was a moderate amount of sunshine, the effect of the light was again slightly to increase the diastase.

The next experiment was continued for 10 days, putrefaction being guarded against by ·2 per cent. potassic cyanide. Two tubes of malt diastase solution were placed side by side in a beaker of water in the laboratory window, one being covered over with black paper. During this time there was a fair amount of sunshine. After 10 days exposure 15 cub. centims. of each were digested with 45 cub. centims. of 1 per cent. starch paste for 45 minutes at 38° C. After titration the weights of cupric oxide yielded were D ·23 grm., L ·09 grm. The 15 cub. centims. malt extract used contained sugar which, when titrated, gave ·08 grm. of cupric oxide. Deducting this, the values for the diastase in D and L were ·15 grm. and ·01 grm. respectively, a destruction in the latter case of 93 per cent.

Other experiments with malt extract gave a considerable destruction of the diastase after exposures lasting from 2 to 5 days.

Experiments with saliva, prepared as in other cases, gave similar results to those obtained with malt diastase.

Two tubes, A and B, were exposed in a beaker of water in the laboratory window for 9 days, B being covered with black paper. 17 cub. centims. of each were then digested with 40 cub. centims. 1 per cent. starch paste at the laboratory temperature for 1 hour. At the end of that time the sugar in each was titrated, the results being, in weights of cupric oxide, A ·08 grm., B ·132 grm., a destruction of the enzyme amounting to 39 per cent.

A further experiment, exposing the solution to diffused light, gave an explanation of the discrepancies hitherto observed.

Two tubes of diluted saliva, prepared as already described, were placed in a beaker of water in the laboratory window, A being exposed to the light, and B covered with a black paper screen. There was a fair amount of sunshine during part of each day for 3 days. The extracts were then examined in the usual way, and for the whole 3 days there was a gradual increase in the diastase. The tubes were then allowed to stand in the window for 8 weeks longer, from November 6th to January 2nd, and they were again examined. The result of the titration of the digestions was then, in weights of cupric oxide, A ·034 grm. B ·0634 grm., a destruction of enzyme amounting to 46 per cent.

The result of this series of experiments thus shows that the action of light on diastase is twofold. When the whole spectrum is employed the effect is the destruction of the enzyme; when only the visible and infra-red portions are used, there is first an increase of diastase, which on longer exposure is destroyed. The destructive rays are mainly those of the ultra-violet, but they are not altogether confined to that region, certain of the visible rays having the same property, but possessing a much feebler power. Certain other rays, whose situation the experiments so far have not accurately determined, have, on the other hand, the power of increasing the amount of diastase in the solution. These may be suspected from the experiments already quoted to be situated at the red end of the spectrum.

An experiment may be quoted here which shows in a striking manner the difference between the two regions of the spectrum. Two cells were taken, one of which (Q), was faced with a quartz plate, the other (G) with a glass one. Each contained 10 cub. centims. of diluted saliva, and a third 10 cub. centims. was reserved in darkness as a standard (D). The two cells were exposed for about 12 hours to the electric arc. 2 cub. centims. of each were then digested for 45 minutes with 25 cub. centims. of 1 per cent. starch paste, boiled and titrated as before. The weights of cupric oxide resulting were: D (standard) ·0695 grm., Q ·05 grm., G ·074 grm. The diastase in Q was diminished therefore by 28 per cent., while that in G was increased by about 6·5 per cent.

Observations tending to localise definitely these different effects will be detailed later.

Effect of Light upon the Diastase in the Living Leaf.

It seemed obvious that of the two effects described, both must play a considerable part in the metabolism of the plant, for though the destruction of diastase appears to be the ultimate effect of the illumination, it is probably preceded by the greater production of the enzyme under the influence of the less refrangible rays, the latter phenomenon being shown to be the first observable under such conditions as allow both to be demonstrated, and to be in magnitude of considerable importance.

The destruction of diastase being, however, the result of illumination by the entire spectrum, the action of the latter upon the living leaf was the next subject of enquiry. The experiments were made upon what is known as the half-leaf plan, and the plant selected was the common scarlet runner, *Phaseolus vulgaris*, that plant having been shown by Brown and Morris to contain a good deal of diastase in its leaves. Leaves were gathered in the early morning, about 5 A.M., and were supported on a frame with their stalks in a test-tube containing water. The leaf of *Phaseolus* is ternate and each leaflet is of considerable size. Half of each of the three leaflets was covered by a piece of blackened paper up to the mid-rib, and the frame was then placed in the sunshine in the open air. The exposures lasted for several hours, and the position of the frame was adjusted repeatedly to face the sun as the day advanced. At the end of the exposure the leaves were killed by exposure to chloroform vapour and dried in the hot-air oven at 35–40° C. The mid-rib and main veins were then cut away, and equal weights of the dried leaf blades on the shaded and unshaded sides of the mid-rib taken for experiment. These were powdered and made into a paste in a mortar and mixed with equal volumes of a 1 per cent. solution of soluble starch, prepared as already described, for the estimation of their relative diastasic powers.

In the first experiment made in this manner the leaf was exposed to a bright sun for 8 hours. The blades without the mid-ribs and main veins were used for the digestions, and the latter were conducted at 40° C. for 22 hours, 60 cub. centims. of the starch solution being used to each weighed portion of the leaf. Equal weights of the shaded and unshaded sides of the blade were tested side by side. After digestion and subsequent titration the weights of cupric oxide were :—

Shaded, ·0618 grm. ; unshaded, ·0498 grm. ; so that a destruction of diastase amounting to rather more than 19 per cent. had taken place.

In a subsequent experiment diffused light was employed instead of direct sunshine. The leaf, mounted and shaded as before, was exposed towards the north to the light from blue sky and white clouds for 8 hours, and then removed and killed with chloroform vapour.

After digestion and titration the weights of cupric oxide were :—

Shaded, ·0538 grm. ; exposed ·0458 grm. ; indicating a destruction of diastase amounting to nearly 15 per cent.

The destruction is seen, on comparing these two experiments, to vary with the intensity of the light.

An experiment was made to test the power of the electric arc upon the living leaf. A vigorous leaf was mounted on the frame as before and exposed for 9 hours to the electric lamp. The temperature reached during the exposure was taken by a maximum thermometer placed in a test-tube of water which was fastened on to the frame by the side of the leaf, and was found never to exceed 37·5° C.

The subsequent treatment was exactly the same as in the experiments conducted in sunlight and detailed above. The final weights of cupric oxide were :—

Shaded, ·0498 grm. ; exposed, ·0448 grm. ; or a diminution of about 10 per cent.

Comparing the destructive effect of the electric light and that of the bright sun, as shown in the experiments just quoted, it appears that the latter is nearly twice as powerful as the former.

Protection of the Diastase in the Living Leaf.

The destruction of diastase, though considerable in the living leaf, is much less than in the extract of malt and in saliva. Either the diastase of the leaf is more resistant than that of the other two extracts, or there is some constituent of the cell contents of the parenchyma that has the power of screening the enzyme from the deleterious rays. Attention is, from this point of view, at once drawn to the chlorophyll as possibly serving this purpose. Besides chlorophyll, however, the light is likely to be interfered with by the protoplasm through which it must pass, and by the proteids contained in the latter and in the cell sap.

As, moreover, the malt extracts and the saliva used contained small amounts of proteids, it became necessary to examine carefully to see whether the action of the light upon the enzyme was indirect, not destroying it, but hindering the manifestation of its activity by interfering with the proteids, with which in some manner, and to some extent, the enzymes are believed to be associated.

There remains still another possible interference, in the acid character of the cell sap of the leaf parenchyma. This is, however, scarcely likely to aid in the destruction of the ferment by light, as it has been found that the presence of a weak acid solution is favourable to the development of almost all ferments and to the activity of many. It was from this reason difficult to submit the influence of this faint acidity to experiment.

An investigation was first made as to the influence of varying amounts of proteid in the illuminated extracts. A solution of egg albumin (white of egg diluted with an equal volume of water), was used throughout this series of experiments. 10 cub. centims. of saliva, prepared as before, were placed in a quartz cell and five drops of the albumin solution added to it. In another similar cell, 10 cub. centims. of the saliva were placed, without any addition of albumin. In a paper-covered bottle were placed a third 10 cub. centims. of the saliva, with five drops of the albumin solution added. They were all exposed to the electric arc for 14 hours. On removal five drops of the albumin were added to the contents of the second quartz cell. Calling these three A, B, and C: A contained diastase illuminated in the presence of considerable albumin, B contained diastase illuminated in its absence, and C served as a control, to give the diastasic power of the saliva when not interfered with by light at all. They were all digested with weak starch paste as in other cases, and after titration, the weights of cupric oxide were: C (standard), ·1116 grm., A, ·1044 grm., and B, ·0943 grm. The extract, without proteid, had hence lost 15·5 per cent. of its diastase, while that which contained it during exposure had only lost 6·5 per cent.

A second experiment was conducted on the same lines, varying the porportion of albumin to saliva. 15 cub. centims. of the latter were taken, and 6 drops of the albumin solution. The cells A, B, and C were prepared as before, and exposed for the same time. The digestion was carried out with twice the relative volume of starch paste, and was prolonged for about three times the period of the first experiment. After titration the weights of cupric oxide were C (standard) ·2093 grm., A (with proteid during exposure) ·1708 grm., B ·0818. In this case the extract without proteid lost 60 per cent. of its diastase, while that which contained it during illumination lost only 18 per cent.

Further experiments, which it would be tedious to narrate in detail, confirmed these results; they all show that the destructive action of the light that has been established is not brought about by action on the proteid, for that a diastasic solution containing a very appreciable quantity of the latter is less and sometimes considerably less injured than one nearly free from it.

That the protection of the diastase in this series of experiments, is to be attributed to the presence of the proteid is demonstrated in the following one, which shows the degree of protection to be in some way proportional to the amount of proteid present.

The extract used was the same saliva as that with which the last experiment was conducted. To 10 cub. centims. in cell A 2 drops of albumin solution were added; to 10 cub. centims. in cell B 1 drop only, and to a third 10 cub. centims. in cell C 2 drops as in A. They were then exposed to the arc light for 9 hours, during which the temperature rose to 29° C. A and B were faced by quartz plates, C with an impervious paper screen.

On removal, 1 drop of the albumin solution was added to B. 5 cub. centims. of each were then added to 60 cub. centims. starch paste (1 per cent.) and they were digested for 37 minutes at 39° C., after which they were boiled, and the products of the hydrolysis estimated by means of FEHLING'S solution, as in other cases. The weights of cupric oxide were C (standard) ·2651 grm., A ·1852 grm., B ·1648 grm. The diastase in B had been reduced 38 per cent., and that in A only 30 per cent., so that the double quantity of proteid in the latter had preserved 8 per cent. of diastase from destruction.

It is evident, however, that some other factors must enter into the causes of the differences observed, as the amount of protection afforded is not in exact proportion to the amount of proteid added. No more definite conclusion can be drawn at present than that proteids have the property of protecting diastase from the destructive rays of the spectrum.

There still remains the question as to the possible protective properties of chlorophyll. The investigation of this body is extremely difficult, as it is insoluble in all watery and neutral solutions, and is changed at once by acids and alkalies. The solvents usually employed for its extraction are alcohol or benzol, and it is very doubtful if these dissolve it unaltered.

Some solution of chlorophyll was prepared by extracting fresh leaves with alcohol, and diluted to such a strength that the absorption band in the green was just visible in the spectroscope. Double cells were constructed consisting of two ebonite rings separated by a quartz plate, and faced by another similar piece of quartz. In the inner cell was placed the diastasic extract, and in the outer one the chlorophyll solution. Two controls were prepared, one with alcohol in the outer cell, and the other with no screen at all. They were exposed to the arc-lamp for 14 hours, and the contents of them separately made to act on starch paste as in other cases. The result of the subsequent titration was to show that while there was a considerable destruction of diastase in the unscreened cell, there was little, if any, in those screened by either alcohol alone or alcohol containing chlorophyll.

A similar experiment made with a solution of chlorophyll in benzol had the same result.

The somewhat unexpected result of finding these solvents opaque to the deleterious rays was confirmed by further experiments. One of these will suffice here. 10 cub.

centims. of salivary diastase solution were placed in a quartz-fronted cell, and screened by alcohol in the outer cell; 10 cub. centims. were placed in a similar cell without a screen, and 10 cub. centims. in a paper-covered cell. These were labelled A, B, and C. They were exposed to the electric arc for 9 hours, the temperature rising to 31° C. 5 cub. centims. of each were then made to act on 25 cub. centims. starch solution for 1 hour 40 minutes. After titration, the weights of cupric oxide were, A, ·0398 grm., B, ·0218 grm., C (standard) ·0438. There was a destruction in B of 50 per cent., but in A of only 9 per cent., so that the alcohol was a very effective screen. Further experiments and observations with the spectroscope led to the conclusion that this reagent is like glass in its opacity to the ultra-violet rays. The protection it affords is not perfect, which is probably attributable to the fact that it allows all the blue and violet rays to pass, for, as we have seen, these are most likely deleterious, though to a less extent than those of the ultra-violet region.

The impossibility at present of preparing an extract of chlorophyll which can be used as a satisfactory screen to a diastasic solution during illumination, renders the proof of its possible protective power very difficult. Various considerations, however, that will be discussed more fully later, point very strongly to such a conclusion.

The Fate of the Rays of Light Absorbed.

In studying the mutual relations of light and diastase it becomes of interest to ascertain what is the fate of the deleterious rays themselves. That they destroy the enzyme is fairly evident. Do they pass on unaltered, or are they reflected, or absorbed and converted into some other form of energy? Some experiments bearing on this point may now be narrated, though a discussion of the matter had better be deferred till the results of the examination of the other parts of the spectrum have been detailed.

The first result of interest in this connection is that the deleterious rays do not pass through a diastasic solution, while the latter is more or less transparent to the beneficial ones. As this is a point of considerable importance, several experiments bearing on it may be quoted.

10 cub. centims. of diluted saliva were placed in the back compartment of a double quartz cell (A), 10 cub. centims. of the same in the front compartment (B), and 10 cub. centims. in a paper-covered cell (C). The three were then exposed to the electric arc for 9 hours, during which a maximum temperature of 31° C. was indicated by the thermometer. 5 cub. centims. of each were then digested with 25 cub. centims. of 1 per cent. starch solution for 1 hour 40 minutes, and then the digestions were titrated as usual.

The weights of cupric oxide found were, A, ·0413 grm., B, ·0218 grm., C, ·0438 grm. Comparing A and C, it is evident that the destruction of diastase indicated in B was almost totally averted in the case of A.

In another experiment both boiled and unboiled extracts were used as screens. Cells were arranged as under :—

A, 15 cub. centims. extract in outer quartz cell.
B, 15 „ „ inner „ behind A.
C, 15 „ boiled and filtered extract in outer quartz cell.
D, 15 „ extract in inner quartz cell behind C.
E, 15 „ „ paper-covered cell, to serve as a standard.

They were exposed to the arc lamp for 9 hours. Then 5 cub. centims. of each were digested with 20 cub. centims. of 1 per cent. solution of soluble starch, as before, at a temperature of 38° C.

The weight of cupric oxide given by the standard E was ·0603 grm. B, screened by the unboiled extract, gave ·0863 grm. ; D, screened by the extract that had been boiled and filtered, gave ·0808 grm. There was no action naturally in C.

The extract in A not only cut off all the deleterious rays, but allowed the beneficial ones to pass. Comparing B with the standard E, the amount of diastase increased 43 per cent. ; comparing also D with the standard, the diastase increased by 34 per cent. The diastase, therefore, whether boiled or unboiled, is opaque to the deleterious rays, while it is only partially so to the beneficial ones.

A further experiment on the screening powers of the boiled extract may be quoted. Cells were arranged as under :—

10 cub. centims. of diluted saliva were placed in the inner compartment and screened by boiled and filtered saliva (A). 10 cub. centims. were placed in a similar cell and screened by water (B); 10 cub. centims. were placed in a paper-covered cell (C). All were illuminated by the arc lamp for fourteen hours. 5 cub. centims. of each were then digested with 20 cub. centims. starch solution (1 per cent.). After titration the weights of cupric oxide were, A, ·1108 grm , B, ·0058 grm., C (standard) ·0888 grm.

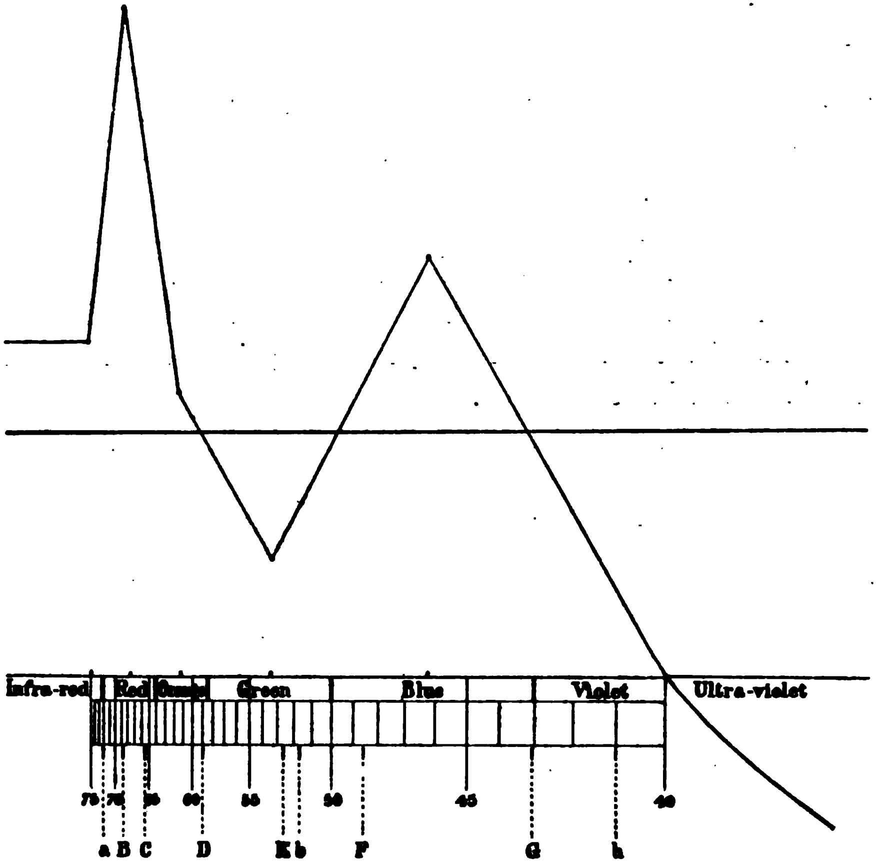
The deleterious rays passed freely through the water, destroying 93 per cent. of the diastase. They failed to pass through the boiled extract, while the beneficial rays increased the diastase 24 per cent.

The deleterious rays seem from these experiments to be absorbed by the diastase, and the power of the latter to absorb them is not closely connected with its fermentative activity. Whatever be the change brought about by boiling in the molecule of the enzyme, it is not of such a nature as utterly to decompose it. When changed by the high temperature, it is still capable of intercepting these rays. To this point reference will be made later.

Localisation of the Beneficial Rays.

In investigating the action of the beneficial rays the method adopted was to eliminate the action of the ultra-violet ones by using glass vessels in which to expose the diastasic solutions, and screening them by other vessels containing various coloured fluids. By the use of appropriate screens the spectrum was divided into seven regions, which may be roughly called the infra-red, red, orange, green, blue, violet, and ultra-violet. Fig. 1. shows the regions of the visible spectrum delimited as will be described; the red includes rays of wave-length 710–645 $\mu\mu$; orange 645–585 $\mu\mu$; green 590–500 $\mu\mu$; blue 500–430 $\mu\mu$; and violet those beyond 430 $\mu\mu$.

Fig. 1.



Curve showing the action of the rays of different wave-length upon the production and destruction of diastase. The ordinates are drawn over the centres of the bands examined, which are indicated upon the spectrum below the curve. The curve above the base-line indicates production, that below it destruction, of diastase.

The screens used were nearly those used by LANDOLT* in his investigations on Dispersion.

They may be described under the colours which they allowed to pass. The red screen was composed of superposed solutions of hexamethyl-pararosanilin (crystal violet), ·03 grm. per litre, and potassic monochromate 10 per cent.

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* LANDOLT, "Methode zur Bestimmung der Rotationsdispersion mit Hülfe von Strahlenfiltern," 'Ber. d. Deut. Chem. Gesell.,' 1894, p. 2872.

The orange screen was made by superposing solutions of nickel sulphate 30 per cent., potassic monochromate 10 per cent., and potassic permanganate about ·2 per cent. The green one consisted of superposed solutions of cupric chloride 60 per cent., and potassic monochromate 10 per cent.; the blue one of a solution of ammonio-cupric sulphate, diluted till it allowed the measured band quoted to pass.

The infra-red rays were examined by using a screen of a solution of iodine in carbon bisulphide.

In every experiment made the rays passing the several screens were carefully ascertained by a spectroscope provided with a wave-length scale.

Many experiments were made with each of the bands so isolated, with the exception of the violet one. It would be tedious to narrate these in detail and the results may therefore be summarised. The accompanying table will show at a glance the percentage increase or diminution in the diastase after an exposure of ten and a half hours duration to the electric arc. As the solutions received with the particular band under investigation the infra-red rays, the ascertained effect of the latter has been deducted in computing the results.

Band examined.	Cupric oxide in grms. reduced by solution exposed to band, after correction for effect of infra-red rays.	Cupric oxide in grms. reduced by unexposed solution.	Increase or diminution of amount of CuO reduced. Diminution indicated by — sign.	Increase or diminution of diastase per cent.	Mean increase or diminution.
Red	·0557	·0354	+·0203	+57·4	
720–640 $\mu\mu$	·0565	·0393	+·0172	+43·7	
	·0921	·0568	+·0353	+62·1	
	·0518	·0343	+·0175	+51·0	+53·5
Orange	·0338	·0323	+·0015	+ 4·6	
640–585 $\mu\mu$	·0296	·0282	+·0014	+ 4·9	+ 4·75
Green	·0285	·0333	—·0048	—14·4	
585–500 $\mu\mu$	·0107	·0129	—·0022	—17·0	—15·7
Blue	·0282	·0242	+·0040	+16·5	
500–430 $\mu\mu$	·0711	·0568	+·0143	+25·1	+20·8

	Cupric oxide reduced by solution exposed to infra-red rays.	Cupric oxide reduced by unexposed solution.	Gain.	Increase of diastase per cent.	Mean.
Infra-red	·0337	·0323	+·0016	+ 5·0	
	·0323	·0282	+·0047	+16·6	+10·8

The diastase used for these experiments was saliva prepared as already described, it being found difficult to prepare the other extracts quite free from colour. The results must be received with a certain amount of caution, as with such different screens it was not at all easy to get the intensity of the light the same in each case, though as much care as possible was taken. Slight differences in intensity in any one case were found, however, not to have a very marked effect during the time of the exposure.

As no screen satisfactorily isolated the violet rays or those beyond wave-length 430 $\mu\mu$, the effect of these can only be a matter of deduction. When experiments were made with the whole visible spectrum and the infra-red, the ultra-violet being excluded by either glass or alcohol, as already detailed, the ultimate effect of the light was deleterious to the enzyme. The infra-red and the visible rays have now been shown to be beneficial, except those lying between wave-lengths 585 and 500 $\mu\mu$, which are slightly deleterious; therefore, the chief injury to the diastase in these experiments must have been caused by the violet rays. They do not appear to be so harmful, however, as the ultra-violet, though when allowed to act for a sufficiently long period, they, like the latter, destroy the whole of the enzyme.

It is possible to represent the effects of all the rays of the light by means of such a curve as is shown in fig. 1, the ordinates of which give approximately the percentage increase or diminution of the diastase in the different parts of the spectrum. The curve rises sharply from the infra-red, reaches a maximum in the red, declines steeply to the orange, crosses the base-line in the green, rises to a second maximum in the blue, and cutting the base-line again at the junction of the blue and violet, becomes negative through the violet and ultra-violet, indicating in these regions a destructive effect.

It has been stated that the deleterious effect of the ultra-violet rays continued and increased after the diastase had been removed from its influence. The same progressive effect was noticed in the case of the improvement set up by the blue rays. In both cases the changes initiated during the exposure continued and increased after the light had ceased to act. The effect of the light consequently is to set up changes of a physical or chemical character in the enzyme or its antecedent, which, when once started, can be maintained without further light influence.

Biological Application of these Influences of Light.

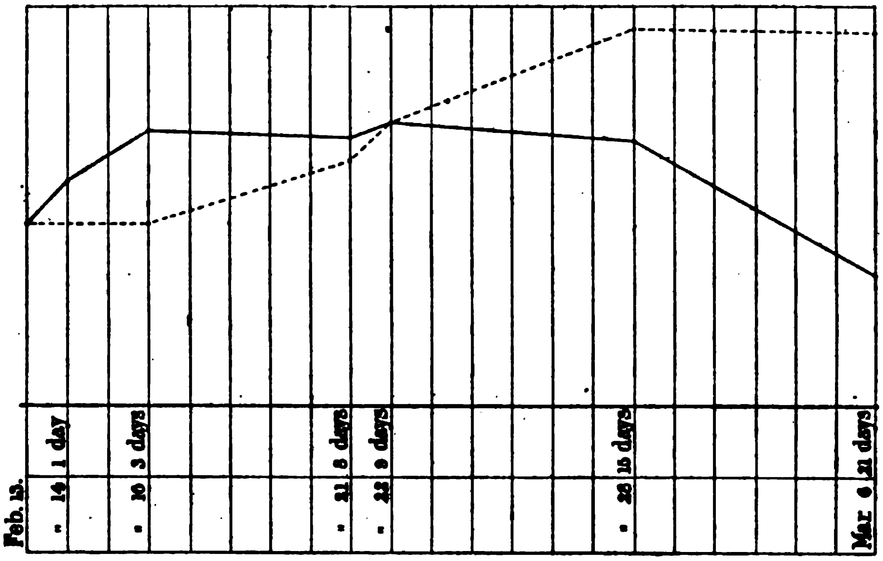
Several considerations of importance in the metabolism of the plant may now be discussed.

The influence of the beneficial rays has been shown to increase the amount of diastase in an extract of malt or in freshly-secreted saliva, or in saliva that has been preserved from decomposition by antiseptics. The fact that the infra-red rays have a definite power in this direction recalls at once the fact that has been established in animal physiology that moderate warmth converts many zymogens into enzymes. This has especially been noted in connection with the secretion of the pancreas. Though the existence of zymogens in the cells of plants has not been at all widely established, yet it has been proved more or less certainly in several cases. The zymogen of human saliva has not hitherto been satisfactorily extracted, either from the secretion or from the salivary gland, but all analogy points to its existence.* The following experiments appear to demonstrate the occurrence of zymogen in the saliva of man, and its similarity to that of the pancreatic juice.

Some saliva was secreted, freed from mucin and considerably diluted, ·2 per cent. of potassic cyanide being added as an antiseptic. It was then divided into two portions, one of which was kept for 21 days in an incubator, the temperature of which was maintained at 38° C, while the other remained at the ordinary laboratory temperature. At certain intervals 2 cub. centims. of each were digested with 20 cub. centims. of 1 per cent. starch paste and the products of hydrolysis titrated with FEHLING's fluid.

The results obtained are given in the following table, and are plotted out in the form of a curve in figure 2.

Fig. 2.



Curve showing the diastasic power of saliva during prolonged exposure to a temperature of 38° C. The abscissæ represent days and the ordinates the amount of enzyme present. The black line indicates the activity of the warmed saliva, the dotted one that of a control kept at the laboratory temperature.

The abscissæ in this curve represent days; the continuous line shows the diastasic power of the warmed, and the dotted line that of the unwarmed saliva.

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* The zymogen of the saliva of the horse has, however, been shown to exist. *Cf.* GOLDSMIDT in 'Zeitschrift f. Physiolog. Chemie.,' vol. 10, p. 273.

Table showing the effect of keeping saliva at 38° C. and at the laboratory temperature.

Time of exposure to 38° C.	Cupric oxide reduced by products of action of 2 cub. centims. of warmed saliva on 20 c.c. starch paste.	Cupric oxide reduced by products of action of 2 cub. centims. of unwarmed saliva on 20 c.c. starch paste.
days	grms.	grms.
1	·0565	·045
3	·0697	·045
8	·067	·062
9	·0706	·0708
15	·066	·095
21	·032	·094

From these experiments, it is probable that the saliva contained, in addition to a certain amount of ptyalin or diastase, a quantity of zymogen, which exposure to a temperature of 38° C. converted into the enzyme completely in about 3 days. Possibly a little remained unchanged until the ninth day. After 15 days at this temperature the enzyme began to change, losing its diastasic power, which at the end of the twenty-first day was much less than at the beginning of the observation. At the temperature of the laboratory, which would be about 18° C., the zymogen did not begin to be converted into the enzyme till after the third day, it then progressed gradually for the rest of the time it was under observation. There was no destruction of the enzyme during the whole of that period, so that the curve of its activity rose somewhat higher than in the case of the warmed extract, in which, during part of the experiment, both processes were at work.

It does not seem from these considerations that it would be rash to infer that the beneficial rays of the infra-red, and hence inferentially of the visible part of the spectrum, convert a zymogen existing in the tissues into diastase.

The rays of the violet and ultra-violet regions are more easily seen to be destructive of the ferment. No other explanation can be admitted, especially when the action of these rays upon bacteria is remembered. The experiments which have been narrated, however, may modify our ideas of what is meant by the term destruction. That the diastasic power is lost is quite clear. The same effect follows when a solution of the enzyme is heated to a temperature of from 70° to 100° C. We have been accustomed to associate this process with a complete decomposition of the molecule of the enzyme. If, however, the conclusions of Fischer* are sound, that the power of an enzyme to hydrolyse the body on which it acts depends upon the configurations of its molecule and of that of the latter, we need not postulate so complete a decomposition. It will be sufficient to explain the cessation of its activity if we imagine the external influence, whether heat or light, to change the configuration of the enzyme, so that it no longer corresponds to the configuration of the molecule of the substance of the hydrolysable material. As **Fischer** puts the relation necessary for hydrolysis, the configuration of the two must be related in some such way as a key is related to the lock which it can turn. If, then, this configuration be interfered with, no hydrolytic action will be possible, even if no further splitting up of the enzyme should take place.

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* E. Fischer, "Einfluss der Configuration auf die Wirkung der Enzyme." 'Ber. d. Deut. Chem. Gesell.,' 27, 2785 (1894).

This view receives some support from the observations already made, that the diastase is opaque to light after it has been boiled, just as it is before. We should imagine such a change as the complete disruption of the molecule of the enzyme would certainly be accompanied by an increase of transparency. As this does not take place, there seems no difficulty in supposing that whatever change is brought about, it is not so extensive as to involve the disruption of the molecule.

When, therefore, a leaf is illuminated by the whole of the spectrum, the order of events seems to be that the beneficial rays convert the zymogen into diastase, and the latter is speedily and continuously changed by the deleterious ones. A light seems to be efficacious for the first process which is weaker than that required for the second.

The means whereby the diastase is partially or completely protected from destruction in the living plant may well receive some attention. It has been shown above that the rate of destruction is less in the living leaf than in an extract containing diastase. The proteids of the leaf have no doubt a considerable power of screening off the deleterious rays and presumably this power is shared by the protoplasm of the cells. The chlorophyll may also be presumed to have a protective effect, though how far this extends may be disputed. The spectrum of chlorophyll is probably without the ultra-violet rays, though no investigation of this point can at present be made. Still, as the amount of chlorophyll in an alcoholic solution is increased, it cuts off more and more of the violet end of the visible spectrum. Even when very little is present, it blocks out the rays beyond 430 $\mu\mu$, which we have seen to be deleterious. It is true that chlorophyll allows most of the green rays to pass through it and these are apparently deleterious. Their effect is, however, but feeble when compared with that of the violet and ultra-violet regions. A reference to the curve, on p. 181, will show that the effect of the green rays in one direction is but little greater than that of the infra-red rays in the other. The powerfully deleterious rays are those beyond 430 $\mu\mu$.

It is, however, probable that the diastase is not situated in the chloroplastid, but in the cell outside it. The destruction that can be observed in the living leaf is inconsistent with the hypothesis that the location of the diastase is in the plastid, for there is strong presumption, as just stated, that chlorophyll cuts off the rays that are deleterious. The increase in the diastase of the leaf would be difficult to understand if it were situated behind a chlorophyll screen, as the spectrum of chlorophyll shows that the latter cuts off especially those rays in the red and in the blue which are active in the conversion of zymogen into enzyme. The proteids afford sufficient protection against the deleterious rays, supposing, as it seems probable we may do, that the place of formation of both enzyme and zymogen is the cell-protoplasm outside the chloroplastid.

In this connection it is interesting to refer to a memoir recently published by PICK,* dealing with the question of the function of the red colour of the sap of certain leaves. This author suggests that certain rays of light hinder the translocation of starch and that the red colour is of importance in shielding the leaf from such rays. He points out in the absence of the red colour there is a great accumulation of starch in the chloroplastids. This cannot be due to increased activity in the process of the deposition of starch there, as the red rays which pass the colour are those which the chlorophyll absorbs and utilises. He further notices that when the leaves receive red light, starch is formed in the spongy, but not in the palisade, parenchyma, owing to the red rays allowing more translocation from the cells of the latter. PICK's conclusions are, however, disputed by EWART,† who thinks that the appearances are due to variations in the rate of carbon assimilation in consequence of alterations in the activity of the chloroplastids under the different conditions PICK describes.

JOHOW‡ has shown that in many tropical plants whose insolation is intense, a red dye is developed in the epidermal cells of the leaf and, in some cases, in their mesophyll cells as well. He proves that the formation of this colouring matter is directly due to the action of the light. When this dye is formed only over the veins and conducting tissues, JOHOW shows that it aids translocation.

The experiments described in this paper indicate the means by which this protective influence, pointed out by both PICK and JOHOW, may be brought about. It is due, not so much to the variation of the action of the chloroplastids, as EWART thinks, but to the effect of the light upon the diastase, the beneficial rays passing to the cells and the deleterious ones being screened off.

In the case of the barley grain, which is the source of the diastase of malt extract, the colouring matter of the ripe grain is a complete screen for the deleterious rays. This was proved by many experiments, in some of which the colouring matter was dissolved in the solution of the diastase, and in others a solution of it was employed as a separate screen superposed during exposure upon the quartz cell containing the extract.

A further consideration of far-reaching importance also arises from the experiments.

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* PICK, "Ueber die Bedeutung des rothen Farbstoffes bei den Phanerogamen und die Beziehungen desselben zur Stärkewanderung," 'Bot. Central.,' vol. 16, pp. 9 to 12.

† EWART, "On Assimilatory Inhibition in Chlorophyllous Plants," 'Journ. Linn. Soc.,' vol. 31.

‡ JOHOW, "Ueber die Beziehungen einiger Eigenschaften der Laubblätter zu den Standortsverhältnissen," 'PRINGSHEIM'S Jahrb.,' vol. 15, p. 299.

There is an absorption of the radiant energy of light, particular rays of which do not pass through the plant-cell, but are absorbed and made available for certain purposes of metabolism. The energy of part of the red and infra-red rays is, as we have seen, very probably employed in converting zymogen into diastase. The absorption of the energy of the ultra-violet and violet rays is equally clear, for they were found not to pass through a solution of diastase so as to affect a second solution placed behind the first. Not only can diastase absorb these rays, but the proteids of the cell have the same power. How they are utilised by the cell the experiments detailed afford no evidence to show, but it does not seem rash to advance the view that we have in vegetable structures a power of absorbing radiant energy which is not connected with the presence and activity of chlorophyll.

The absorption of energy by the vegetable organism without the assistance of a chlorophyll apparatus has already received some attention in recent years. ENGELMANN* has shown that in certain bacteria heat rays are of use in the construction of organic substance. This is, however, probably effected by means of a pigment by which the heat rays are absorbed, much as are the light rays by chlorophyll. There is, at any rate, a fixation of energy in the plant which is derived from the rays of the infra-red region of the spectrum.

PFEFFER† shows further that the energy of pressure and of tension can also be utilised by the vegetable organism. The experiments of WINOGRADSKI‡ on the nitrifying bacteria also show the formation of organic material from inorganic bodies without the agency of chlorophyll. The conditions under which this is carried out point to the absorption of energy from the chemical decompositions which accompany or precede the nitrification. The sulphur bacteria appear to carry on a similar constructive process, obtaining energy from the oxidation of sulphur or sulphuretted hydrogen, and the iron bacteria by oxidation of ferrous oxide.

The absorption of the energy of an electric current appears possible also, though but few observations have been made upon it. SPESCHNEW cultivated some cruciferous and umbelliferous plants in a bed of earth, at one end of which a copper plate, and at the other end an iron one, had been buried a little below the surface, their faces being parallel to each other. When these plates were connected by a wire, a current passed and traversed the earth between them. Plants growing in the course of the current were much more vigorous than others grown for the purpose of a control in an adjoining part of the same bed. It is at least possible that the greater growth in the former case was due to the fixation of a portion of the energy of the current.§

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* ENGELMANN, 'Bot. Zeit.,' 1888.

† PFEFFER, "Zur Energetik der Pflanze," Leipzig, 1892.

‡ WINOGRADSKI, "Recherches sur l'organisme de la nitrification," 1890, 1891. 'Annales de l'Institut Pasteur.'

§ [Since this paper was put in type my attention has been called by Professor MARSHALL WARD to an

It is possible, further, that we may base an argument on these experiments against the proteid nature of diastase. The composition of the enzymes is a much-disputed question, and only recently **Osborne**[*] has advanced the view that the diastase of barley is probably to be identified with one of the proteids of the grain. The change brought about in the diastase by the ultra-violet rays militates to a certain extent against that view. So far as we know, light brings about no change in the composition of proteids, while it evidently does alter, at least, the configuration of diastase to a very marked extent.

Summary.

It has now been established by **Brown** and **Morris** that there is a diminution in the amount of diastase in foliage leaves after a period of bright illumination. This has been explained by them as connected with variations in formation and consumption under different conditions, but the possibility remains that there may be a destruction of the enzyme by light comparable to the destruction of bacterial life under the same conditions.

Various diastasic solutions and living leaves were exposed by the writer for different times to the light, either of the sun or the electric arc, and their diastasic power ascertained subsequently by digesting measured quantities with starch solutions, the experiments being in all cases carefully controlled. Various means of exposure were adopted, so that either the total rays, or those of the infra-red, or those of the whole or definite parts of the visible spectrum were tested independently.

The effect of the whole spectrum was to diminish the diastase in the solution. Malt diastase lost on the average 68 per cent. in 14 hours; saliva 45 per cent., and leaf diastase in solution 8 per cent. In the living leaf there was a destruction of diastase amounting to 15 per cent.

When the ultra-violet rays were excluded by using glass vessels the first effect was to increase the diastase from 15 to 20 per cent. This increase was succeeded, after prolonged exposure with antiseptic precautions, by almost complete destruction.

The two ends of the spectrum were thus found to have opposite effects. The

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important memoir recently published by MM. **Laurent**, **Marchal**, and **Carpiaux**, in which the authors detail some experiments made in 1895 and 1896, which prove not only the absorption of the energy of the rays of the violet and ultra-violet regions, but further, that these rays are concerned especially in the construction of nitrogen compounds from the nitrates or ammonia compounds absorbed by the plants, while the intervention of the chlorophyll apparatus is unnecessary for this purpose. "Recherches expérimentales sur l'assimilation de l'azote ammoniacal et de l'azote nitrique par les plantes supérieures." **Laurent**, **Marchal** et **Carpiaux**. 'Bull. de l'Acad. Roy. de Belgique.' Third series, vol. 32, No. 12, pp. 815–865, 1896.—J. **Reynolds Green**.]

[*] **Osborne**, "The Chemical Nature of Diastase," 'Jour. of the Amer. Chem. Soc.,' vol. 17, 1895, p. 587.

deleterious rays were not, however, confined to the ultra-violet, but some of them were found to be present in the visible region.

On the whole the solar rays were more deleterious than those of the electric arc.

In the living leaf a certain protection is afforded from the action of the light by the proteids in the cells. The effect of adding proteid to diastasic solutions before exposure to the electric light is to reduce the destruction, the protection being greater as the amount of proteid is increased. It is not improbable that chlorophyll may exert the same protective influence, but this cannot be definitely ascertained as the solvents which extract it are largely opaque to the deleterious rays.

The latter rays do not pass through the diastasic solution unchanged, whether the diastase is active or has been destroyed by boiling. There is thus an absorption of radiant energy. No statement can be made as to the fate of the deleterious rays.

The rays which are beneficial are of use to the plant in transforming zymogen into enzyme. In the paper, experiments are quoted bearing on this point, the effect of light being compared with that of prolonged exposure to a temperature of 38° C., with which it coincides.

By a series of experiments the beneficial rays were localised chiefly in the red, orange and blue regions, the green and violet having a similar effect to those of the ultra-violet region, but being much less efficient. The relative increase or diminution of diastasic power caused by the different regions is as follows :—Infra-red, + 10·8 red, + 53·5 ; orange, + 4·75 ; green, — 15·7 ; blue, + 20·8. Those of the violet and ultra-violet regions were deleterious, but their energy could not be measured. The paper contains a curve giving a representation of the light effects and showing the delimitation of the several regions examined.

The effect of the different rays is not produced only during the action of the light, but continues after the extract is removed from illumination.

The experiments lend support to the view that in the cells of the leaf the enzyme is located in the protoplasm or the vacuole, and not in the chloroplastids.

They go further to establish the conclusion that in the vegetable cell there is a power of absorbing the radiant energy of the solar rays apart from the existence of the chlorophyll apparatus.

V. *Investigations into the Segmental Representation of Movements in the Lumbar Region of the Mammalian Spinal Cord.—Excitation of the Spinal Cord, and Direct Excitation of the Spinal Nerve Roots.*

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INTRODUCTION.

THE following research was carried out in consequence of suggestions made to me by Professor VICTOR HORSLEY, to whom I wish to express my thanks for placing the facilities of his laboratory at my disposal, and for his advice and criticisms during the prosecution of the work and in the preparation of the paper. I also wish to return my best thanks to Professor JOHANNES GAD, in whose laboratory the first part of the work was carried out, for his ever-ready and constant help and advice. I have further to thank my friend Dr. RISIEN RUSSELL for his kindness in assisting me in some of my earlier experiments on the monkey.

The researches were undertaken with the view of throwing light upon the degree to which certain movements or, speaking more precisely, sensori-motor (kinæsthetic) phenomena are represented in any given segment of the lumbo-sacral region of the mammalian spinal cord, and further what relationship exists between the representation of one movement and that of another. It is clear that at least three methods suggest themselves as means whereby this problem may be attacked, *e.g.*, (1) the excitation method, (2) the method of exclusion by ablation, and (3) the so-called degeneration method. Of these Nos. (2) and (3) have been already in part employed (No. (2) SHERRINGTON, RISIEN RUSSELL, No. (3) GRÜNBAUM), but believing that with suitable precautions more exact localisation could be obtained by the excitation method, I have so far adopted that alone.

Of necessity a number of side issues of interest and importance have presented themselves, and have been considered and studied so far as was consistent with the pursuit of the general plan of the research.

In this, the first part of the work, the procedure adopted was that of exciting either root of a given segment and observing the resulting movements. Later on, as described in the second part, the segments of the cord were directly excited, and the movements evoked recorded.

HISTORICAL INTRODUCTION.

Although a series of laborious investigations have been carried out to determine the localisation of certain movements and the physiological relationship of various muscles in and to definite segments of the spinal cord by **FERRIER** and **YEO**, **BERT** and **MARCACCI**, **FORGUE**, **SHERRINGTON**, and **RUSSELL**, all these were limited (controlled by exclusion experiments) to stimulation of the motor roots. I am only aware of one antecedent localisation experiment carried out by stimulation of the posterior roots. This is one by **SHERRINGTON**, 'Jl. Physiol.' vol. 13, p. 730, in which he endeavoured to obtain from the posterior root the same effect which is got by excitation of the anterior root, but he came to the conclusion from this experiment that the representation of movement in the two cases did not correspond. Nor can I find any record of the direct excitation of the surface of the cord for the localisation of movement. Of course experiments on the conducting channels are not now under consideration. Inasmuch as the present research is limited to the lumbo-sacral region, it is only necessary to summarise in tabular form the localisation already obtained by excitation of the anterior roots.

METHODS OF INVESTIGATION AND PRECAUTIONS OBSERVED.

(*a*) *Species of Animal.*

The animals chiefly employed were the dog and monkey (*Macacus sinicus* and *rhesus*). The rabbit was tried in a few instances, and the results obtained with it, in so far as they went, agreed with those in the dog and monkey; but the animals succumbed so easily to shock that they did not prove suitable for these experiments. The cat, however, in the cases experimented upon, answered admirably.

(*b*) *Anæsthetic.*

The narcotic agents used were morphia and ether. It is necessary to dwell for a moment on the general question of narcosis, considering that the whole of the question investigated involves the active condition of the spinal nerve centres.

The anæsthesia was pushed to a profound degree for the performance of the first stage of the operation, viz., exposure and division of the spinal cord. Inasmuch as the whole of the body below the section was forthwith anæsthetic and analgesic, the necessity of deep narcosis no longer existed, and it was consequently possible to obtain the most important results with a relatively slight degree of narcosis.

Proceeding now to special considerations of the narcosis with different agents :—

1. *Morphia.* Morphia, as is well known, in moderate doses heightens reflex action and producing analgesia. It was, therefore, a very valuable narcotic in the present research. It was invariably employed in the dog in doses of from 15 to 20 c. grm., and was given hypodermically about ten minutes before the commencement of the operation. Ether was then administered, and the animal kept at any degree of narcosis required by its means.

2. *Ether.* The employment of ether as a general narcotic was found very useful on account of the ease with which the intensity of the narcosis of the centres could be regulated. It introduces, however, a complication now well known, viz., its differential action on antagonistic groups of muscles (*e.g.*, flexors, extensors, &c., &c.). Since this differential influence is only observed where considerable doses are administered, it could not be regarded as a factor in the present investigation; for in the large majority of experiments it was not found necessary to administer any after the section of the cord above the seat of operation. At the termination of the experiment, the animal was given an overdose of chloroform, and hence from first to last the causation of pain was entirely avoided.

OPERATIVE PROCEDURE.

Exposure of Cord.—Division of Cord and Isolation of Segments.

The cord was exposed with due observation of well-known precautions. (For full details, see GOTCH and HORSLEY, Phil. Trans., B., Vol. 182, 1891.)

The animal was kept warm by being placed on a hot-water tin and covered as much as possible.

In some cases, the spinal cord and roots were stimulated at first in continuity. In others, before proceeding to experiment, the spinal cord was completely divided at a distance varying from two to eight segments above the part experimented upon. For the section of the cord, the anæsthesia was profoundly pushed; and then, by means of a sharp knife, the spinal cord was cut completely through in its sheath of dura mater, and a little amadou pressed gently into the bleeding points. In this way the hæmorrhage seemed to give little trouble. In other cases, the dura mater was first opened longitudinally, and a fine cataract knife being passed beneath the dorsal vessels, the cord was cut through, leaving them intact. This method answered extremely well.

METHOD OF EXCITATION.

1. *Electrical.*

Apparatus.

A single Daniell cell was used and supplied to a DU BOIS-REYMOND'S inductorium of the usual type, the secondary coil being generally 20 centims. from the primary. The electrodes attached to the secondary coil consisted of fine closely-approximated platinum points, usually 1 millim., rarely 2 millims. apart. The duration of excitation was as a rule momentary, and never exceeded 1–2 seconds.

(a.) *Excitation of Nerve Roots.*

The nerve roots were raised in the air, and the electrodes usually applied so that the direction of the exciting current was transverse to the nerve fibres.

(b.) *Excitation of the Spinal Cord.*

Direct electrical excitation of the surface of the spinal cord itself may, as a method of precision, not at first sight commend itself, but a brief experience, under the direction of Professor GAD, soon showed that it is a remarkably easy thing to obtain perfectly constant and accurate results, control of which is also readily effected. The surface of the cord was gently dabbed with small wool swabs (kept in warm saline solution and squeezed dry) before the electrodes were applied. The duration of excitation was always very brief, not exceeding one second, and attention was given to the minimal response. The value of the method may be estimated by a consideration of the following facts. On stimulating the surface of the spinal cord, as already mentioned, movement was always elicited in the leg on the side stimulated, when the electrode was applied to the surface of the *posterior* column, but never, as far as I was able to see, could movement be obtained by the application of this strength or even considerably greater strength of stimulus to the *lateral* or *anterior* columns when adequate precautions were taken to prevent the direct spread of the current to the neighbouring root fibres. It was easy enough to produce movement on stimulating the surface of the anterior columns if the motor fibres, which run almost vertically for several segments of the outer surface of the cord in this region, were not eliminated, but when all precautions were carefully taken, I could not convince myself that movement resulted from application of a current to the surface of the anterior or lateral columns, whereas that elicited from stimulating the posterior columns was always marked and quite definite, and merely depended in intensity upon the conditions stated below. For instance, applying the electrodes to the surface of the postero-external column in the 5th lumbar segment of the dog on the left side produced lateral flexion of the spinal column of the same side, flexion and adduction of the hip, flexion of the knee and toes, and movement in the tail (flexion to the same side). But of the facts observed the chief was the very local effect which would be obtained by varying the point stimulated. Thus stimulation of a point 1 millim. centrally or laterally of a given point often produced an entirely different resulting movement, or no response at all, which fact is clearly of much importance in showing that with the above strength of current the restriction of the stimulus to one point must be sufficiently well obtained.

2. *Mechanical.*

As a means of controlling the observations derived from electrical excitation, mechanical stimulation was sometimes employed in examining the nerve roots, and was evoked by pinching the tissues with fine forceps. The results obtained were precisely the same.

The results obtained by direct excitation of the cord will now be grouped as follows :—

(1.) Gross localisation according to the general structure of the cord.

(2.) Minute localisation within the excitable area.

RESULTS OBTAINED BY DIRECT EXCITATION OF THE SPINAL CORD (DOG).

Gross Localisation.

(a.) *Area Excitable.*

The excitable area of the surface of the cord itself is the postero-external column. Stimulation of the column of GOLL as a rule produced no movement except in the lower lumbar region, where that column is either very narrow or entirely absent. Thus at about the level of the 7th lumbar nerve stimulation of the posterior column in the middle line produced movement, namely flexion of the hip, flexion of the ankle, and flexion of the toes.

It is probable that the effect is here due to the stimulus directly spreading to the fibres of the postero-external column owing to the narrowness of the intervening portion of GOLL's column. As already observed, excitation of the antero-lateral column with any stimulus less than thrice that adequate for the posterior columns was without result. It seems, therefore, proper to conclude that the postero-external column can alone be considered for the purposes of minute localisation as excitable on its surface as compared with the other column of the cord.

The reason for this probably is, that the postero-external columns are made up almost entirely of the branches (ascending, descending, and collateral) of the posterior roots, and that these are at and near the surface of the cord.

(b.) *Unilaterality.*

In the large majority (91·5 per cent.) of experiments on animals, the fact was strikingly evident that the movements produced were limited to the side stimulated. Only in three dogs in thirty-five (8·5 per cent.) could movement be produced in both legs—*i.e.*, sides—by stimulating only one side of the spinal cord. That this double effect was not due to the direct spreading of the current to the posterior column of the other side was proved in each case by the fact that application of the electrode to a point or points nearer the middle line and at the same level produced no movement whatever. In one of the cases the same double result was obtained from stimulating one posterior column even when the spinal cord had been split completely through at the anterior and posterior fissures as far down as three segments below the point where the cord was excited. In this particular preparation the cord was transversely divided* just above the point first stimulated, and after vertical splitting the halves were drawn apart, but on then splitting the cord through another segment the double effect vanished, though the lateral effect remained. Such double effects, therefore, are attributable to (1) the commissural connections of the two halves of the cord and (2) the degree of excitability of the cord fibres in particular cases.

(c.) *Vertical Extent of the Spinal Cord in the Dog; Movement in the Lower Limb can be produced.*

In the dog movements in the lower limb can be produced from stimulation of BURDACH's column along the following vertical extent, from the upper border of the 13th† dorsal segment to the lower border of the 1st sacral segment.

Movements.

Flexion and adduction of the hip from the upper border of the 13th dorsal segment to the lower border of the 6th lumbar segment.

Flexion of the knee from the lower border of the 1st lumbar segment to the lower border of the 7th lumbar segment.

Flexion of the ankle from the lower border of the 1st lumbar segment to the upper border of the 7th lumbar segment.

Flexion of the toes from the upper border of the 1st lumbar segment to the upper border of the 1st sacral segment.

Closure and protrusion of anus from the lower border of the 4th lumbar segment to the upper border of the 2nd sacral segment.

Movement of tail from the upper border of the 5th lumbar segment to the lower end of the sacral region.

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* The description of the result obtained after dividing the cord to separate it from the higher centres is given on the next page.

† The term segment is used here in the sense given to it by Professor SCHÄFER (QUAIN'S 'Anatomy,' 10th edit., vol. 3, Part I., p. 3), namely, the portion of cord which is in anatomical relation with any given root, and which is therefore limited above and below by imaginary transverse lines, drawn arbitrarily at a point midway between the centres of attachment of adjoining roots. These imaginary lines are termed in this paper, for the sake of clearer description, the upper and lower borders respectively.

From this it will be seen that the various areas in the postero-external column, the stimulation of which on the surface of the cord produces movements in the limbs, anus, perineum, and tail, all overlap one another, but that, on the whole, the hip area is a little nearer the cerebrum than that for the toes, and the area for the knee more proximal than that for the foot, and so on; but the whole representation of the joints is so brought together within the narrow space of the lumbar enlargement that no sharp division of the points of maximal representation is possible. This much ascertained, it was necessary to still further differentiate the foci of representation of the movements resulting from direct stimulation of the cord by a control experiment.

For this purpose Professor GAD suggested the application of a fine hot needle transversely to the path to be divided, and by this means it was quite easy to cut any particular strand of fibres without pressing on surrounding points and without causing hæmorrhage of any kind. For instance, in a dog under ether and conditions as described above application of the electrodes to the postero-external column at any point of the 4th or 6th lumbar segment produced flexion of the hip and knee, and these movements seemed identical in every respect; then by gentle application of the red-hot needle the postero-external column was divided across in the centre of the 5th segment, after which stimulation of the 4th segment only evoked flexion of the hip, whereas stimulation of the 6th segment produced only flexion of the knee. This fact is of great interest, especially in relation with the observations of RAMON-Y-CAJAL and BARBACCI, because it is so plain that movement which results from stimulation of the posterior external column must be brought about not only by means of stimulation of the short reflex arc fibres in the same segment, but also by means of stimulation of the intersegmental (see also below) fibres (RAMON-Y-CAJAL), and in all probability by stimulation either directly or indirectly of the collateral fibres as well.

(d.) *Effect of transversely dividing the Cord above the Lumbar Enlargement.*

It was expected, and not without reason, as the experiments detailed show, that in excitation of the uninjured spinal cord the influence of the higher (cerebral) centres could be readily and adequately abolished by the employment of ether narcosis. To render, however, the conditions more absolute towards the end of the experiment, a complete transverse section of the cord was made at a variable distance, usually from two to six segments above the part investigated, and the excitation repeated.

For this purpose the animal was placed under deeper narcosis by ether, so as to diminish shock as much as possible, and then the cord and vessels were completely divided by a sharp cataract knife, the two parts of the cord retracting so that a gap of at least 6 millims. to 10 millims. resulted. The hæmorrhage was usually sharp, but, by the application of a little amadou to the bleeding points, it almost immediately ceased and gave no further trouble. With a view to diminish the hæmorrhage and to maintain the circulation in the cord, a cataract knife was later passed under the dorsal vessels, and then by cutting forwards the cord was left with as good a circulation as possible. This method answered very well.

The only result observed to follow such separation of the cord from the brain, upon the movement elicited as above described, was one of increased excitability. The limits described (p. 196) (areas of vertical extent) were found to prevail precisely, and the cord was excitable, quite up to the level of the section, a smaller stimulus being necessary to produce the same movements as before. For instance, the distance of the secondary from the primary coil before section of the cord being 30 millims. for an adequate stimulus, the same result was obtained after division of the cord with secondary coil 50 millims. or 60 millims. from the primary. As regards the above-described influence of section, other conditions, as is well known, exerted an obvious effect. Thus, for instance, increasing the narcosis diminished the excitability, or even removed it; and, on the other hand, repeated stimulation either of the cord or the posterior nerve roots (see below) increased the excitability.

Further, if the cord were not irrigated from time to time with saline solution or other suitable agent, but allowed to dry, then for a time its excitability was increased. Again, the application of the red-hot needles described above gave rise to an increase of excitability.

As far as was compatible with the performance of the foregoing experiments, the knee-jerks were investigated, and it was found, of course, that with the cord intact they were present, but were influenced by the conditions which increased or diminished the excitability of the cord. When the cord was cut through in the dorsal region, and it was perfectly obvious from the gap of half-an-inch or more between the two portions that no direct communication could exist between the two parts (and therefore between the lumbar region and the brain), the knee-jerks, nevertheless, persisted in nearly every instance (in some thirty animals), and were much more active and more readily elicited than before the section of the cord. Sometimes soon after section the knee-jerks could not be elicited, but by waiting a few minutes to allow the shock to diminish or pass away they could almost invariably be obtained, and that in a more active condition than before the section. These observations, it will be remembered, were made on the dog alone.

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Monkey. Anterior roots.	Ferrier and Yeo, 1881, 'Proc. Roy. Soc.,' vol. 32, p. 18.	Forgue, 1883, 'Distribution des Racines dans les Muscles des membres.'	Sherrington, 1892, 'Journ. Phys.,' vol. 13, No. 6, p. 648.	Russell, 1893, 'Proc. Roy. Soc.,' vol. 54, p. 254.
1st post thoracic (lumbar).	Flank muscle only	..	Retraction of abdominal wall .	No intrinsic movement in the limb.
2nd ditto . . .	Flank muscle only	..	Retraction of abdominal wall, slight flexion of the hip.	No intrinsic movement in the limb.
3rd ditto . . .	Muscles of the flank—not of leg (0 cruris).	..	Lower part of abdominal wall, flexion of hip, slight flexion knee, slight ext. rotation thigh.	Slight flexion at the hip.
4th ditto . . .	Flexion of thigh, extension of leg—ilio psoas—partorius, adductors and extensors cruris.	Flexion of thigh, extension "de la jambe," adduction.	Contraction of lower part abd. wall, flexion and adduction of hip, slight ext. rotation of thigh.	Flexion at the hip, adduction of thigh, extension of knee.
5th ditto . . .	Extension of thigh, extension of leg, pointing of great toe, raising of outer edge of foot (= gluteal adductors, ext. cruris, peronius longus).	Ext. (not of hip) "de la jambe," adduction of thigh, dorsiflexion of ankle, inversion of sole.	Flexion of hip, adduction of thigh, extension of knee, slight flexion of ankle, slight inversion of sole, slight extension of hallux.	Extension of whole limb, adduction and int. rotation of thigh, dorsiflexion of the foot.
6th ditto (5th lumbar in man).	Ext. rotation of thigh, flexion of leg with inward rotation, plantar flexion of the foot, flexion of hallux and toes at their distal phalanges, outer edge of foot somewhat raised (= hamstrings, sural muscles, long flexors, tibialis ant. and post. peronei, and extensors of the toes).	Ext. of thigh and ext. rot., slight flexion of knee, eversion of sole, flexion of digits at "au niveau des 2nds phalanges."	Extension of hip, adduction of thigh, weak flexion or ext. of knee, flexion of ankle, inversion of sole, extension of toes, weak adduction of hallux.	Extension of hip, adduction and ext. rotation of thigh, flexion of knee with ankle at right angles and everted flexion of distal joints of hallux and digits.
7th ditto (1st sacral in man).	Flexion of the leg (hamstrings), plantar flexion of foot, abduction of the hallux, flexion of toes at proximal phalanges, flexion of toes hallux at the distal phalanges, slight ext. rotation of thigh.	Flexion of knee, extension of ankle, flexion of digits, inversion of sole.	Extension of hip, slight ext. rot. of thigh, flexion of knee, extension of ankle, eversion of sole, flexion of digits with strong adduction of hallux, depression of root of tail.	Extension of hip, flexion of knee, extension of ankle, inversion of the sole, flexion of metacarpophalangeal joint with the hallux flexed and adducted beneath the flexed digits.
8th ditto (1st sacral) (2nd sacral in man).	Adduction of flexion of hallux (basal phalanx), plain of proximal phalange of toes, slight separation and ext. of distal phalanges, tail moves to same side.	Adduction and flexion of hallux, flexion of digits (terminal phalanges), and bringing together of fingers.	Slight ext. rot. of thigh, ext. of hip, flexion of knee, strong ext. at ankle, strong flex. and add. of hallux, flex. of digits in internal position.	Interosseal flexion of the digits, flexion and adduction of the hallux.
9th ditto (2nd, 3rd, and 4th sacral).	Movements in tail only (six times experimented).	Tail only.	Slight ext. rot. thigh, flex. and add. of hallux, flex. of digits.	No movement in the limb.

Peyer, Krause (Kronenberg; and Berol brachial of rabbit). Johannes Muller and Van Deen experimented on crural plexus of frog.

Movement elicited by excitation of posterior roots.	
12th dorsal posterior . .	Flexion of the side and psoas.
13th dorsal posterior . .	Flexion of side, psoas, and slight flexion of hip (once).
1st lumbar posterior . .	Flexion of side, slight flexion of hip, contraction of hamstrings.
2nd lumbar posterior . .	Flexion of side and abdominal muscles, flexion of hip, contraction of hamstrings, dorsal flexion of ankle, flexion toes, specially 3rd and 4th, tail to same side.
3rd lumbar posterior . .	Flexion of side, flexion and adduction of hip, dorsal flexion ankle, flexion toes and tails.
4th lumbar posterior . .	Flexion of side, flexion and adduction of hip, ext. knee, hamstrings, flexion ankle, slight flexion toes and tail.
5th lumbar posterior . .	Flexion of side, tensor fasciæ latæ and rectus femoris, flexion and adduction of hip, flexion ankle, slight flexion toes and tail.
6th lumbar posterior . .	Adduction and flexion hip, hamstrings, slight extension knee, flexion ankle, and inversion of the foot and movement of tail.
7th lumbar posterior . .	Slight rotation out of femur, hamstrings, and glutei, flexion of knee, slight dorsal flexion of ankle, occasional slight ext. of ankle, flex. toes and big toe, eversion of sole of foot and movement in middle and tip of tail.
1st sacral posterior . .	Extension of ankle, flexion of toes, movement in tail.
2nd sacral posterior . .	Slight flexion toes, movement in tail.
3rd sacral posterior . .	No movement in limb, but only in tail.

RESULTS OF EXPERIMENTS UPON THE SPINAL CORD IN THE MONKEY.

Method.

The experiments were carried out in exactly the same manner as detailed above. The monkey was anæsthetised with ether. As is well known, ether answers admirably as a narcotic with monkeys, and it is easy to regulate the depth of narcosis to any degree. Previous to dividing the spinal cord, profound narcosis was produced in order to diminish the shock as much as possible. In most cases after division of the cord, the monkey remained in a drowsy condition and required no fresh anæsthetic, but ether was always given on any indication of restlessness. The operation was performed in the usual way and as already described above. As in the case of the dog, the experiment was divided into two chief stages; the first in which the spinal cord and roots were investigated while every structure was intact, and the second in which the spinal cord or various anterior roots were divided during the progress of the experiment. The only change produced by section of the spinal cord was to increase the excitability of the cord and roots below the section.

In the spinal cord of the monkey, stimulation produced the same general results as in the dog. I could not observe any movement elicited from stimulating any part of the surface of the cord, except from that of the postero-external column; this was always easily and constantly obtained. The vertical extent of this representation of movement of the lower limb in this column was limited above by, on the average, the upper border of the 13th dorsal segment, and below by the level of attachment of the 2nd sacral root to the spinal cord. Movement occurred after a very short latent period, and took the form always of flexion and adduction of the hip, flexion of the

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knee, ankle and toes, with lateral flexion of the side and rumbling of the bowels, though it depended on the position of the electrode and the strength of stimulus whether only a part or the whole of these movements resulted.

Starting above the upper limit of representation, say at the 10th dorsal segment, and then working downwards, the first movement obtained is lateral flexion of the side. The animal moves as if he had suddenly been poked in the side, the flexion of the spine being towards the side stimulated. The first movement observed in the muscles of the hip was always flexion and never extension, though adduction is not infrequently added, and occasionally rotation of the hip. This movement of the hip can be obtained on stimulating the posterior external column anywhere from the level of the 13th dorsal segment of the spinal cord, as low as the attachment of the 6th lumbar nerve. The area, stimulation of which causes flexion of the toes, extends from the 2nd lumbar segment to the upper part of the 7th lumbar segment, and the area similarly for flexion of the knee commences about half a segment lower. Rumbling in the intestine was produced occasionally by stimulation of a point, or points in the postero-external column at about the level of the 5th or 6th lumbar segment, and the similar area for causing movement in the perinæum and closure and protrusion of the anus was a little more extensive and a little lower down, whilst stimulating at any level from the 3rd lumbar to the 3rd sacral produced movement in the tail. An interesting point in connection with the latter was, that according to the position of application of the (minimal) stimulus did the base, the middle portion, or the tip of the tail move, the higher in the cord the point stimulated, the nearer to the base of the tail was the portion of tail which moved, but if the stimulus was a strong one, the whole of the tail moved. The chief movement occurred to the side in which the posterior external column had been stimulated, except occasionally in the lower part of the cord where the column of GOLL was practically or entirely absent. Stimulation in the middle line caused, usually, depression of the tail, though occasionally elevation of the tail occurred, but the more laterally was the stimulus placed on the posterior external column, the more did the tail move to that side.

Similarly with regard to the lateral extent of the areas mentioned above, whereas of course a strong stimulus caused movement in all the parts named, nevertheless in each case it was quite definite that the area for the tail was nearer the middle line than that for the hamstrings, the area for the hamstrings nearer the middle line than that for flexion of the hip, and this median of that area stimulation of which caused lateral flexion of the side. That the posterior fibres as they ascend in the cord are placed nearer the middle line than those entering the cord higher up, and so on, of course, is now well known anatomically, but the arrangement has not hitherto been demonstrated functionally, nor the fact that stimulation of certain paths or areas in the posterior external column gives definite movements in definite parts. These areas seem quite constant, and, of course, overlap one another in their vertical, if not in their lateral extent. That this is so would, of course, be anticipated from consideration of the necessarily complex structure of such an organ as the spinal cord, and absolutely sharply-defined areas could not therefore be expected in each animal. That variations in the origin and functions of the nerve roots occur even in the same species, has been shown by the investigations of **Ferrier** and **Yeo**, and especially more recently of **Sherrington** and **Russell**. In this latter connection the experiment, detailed at page 204, is of particular importance, for it proves that not only can there be a variation in different animals, but also in corresponding nerves of the two sides, since it was shown that a stimulus applied to the left 2nd sacral anterior root produced no visible movement whatever in the lower limb, yet the same stimulus caused invariably and obviously a distinct movement in the right digits when applied to the right 2nd sacral nerve.

As in the dog, the knee jerks were occasionally tested, and were found not only present but even exaggerated after the cord had been divided, and this agrees with the previous results obtained by **Sherrington** and **Russell**.

Similarly, section of the spinal cord caused the heightening of excitability as observed in the dog, and the lower portion of the cord was excitable as high as within a very narrow margin of the cord section. Stimulation of the same points also gave the same results as before section, though with regard to the posterior roots (see below) it was found that movement obtained through stimulation of any given posterior root was abolished a variable distance, usually from 1 to 3 segments, below the section, and that the more oblique the position of the posterior root in contact with the cord, as, for example, in the lower part of the cord, the greater would be the interval affected in this manner. For example, section of the spinal cord at the level of, say, the upper part of the 2nd lumbar segment abolished movement previously elicited by excitation of the 2nd posterior root and gave partial results on exciting the 3rd posterior root, whilst the effects of stimulation of the 4th posterior root was unaffected. Moreover, lower down, *e.g.*, after section of the cord at the level of the upper part of the 5th lumbar segment where the nerves enter much more obliquely, the results of excitation of the 5th and 6th posterior roots are abolished, and not merely diminished, and those elicited from the 7th may be decreased.

On the Production of Movement by Stimulation of the Anterior and Posterior Spinal Roots in the Monkey.

The general results obtained by excitation of the spinal roots in the monkey were precisely the same as those in the dog and need not be repeated, but certain differences were observed and with any other points of importance will be more considered. First of all, the effects observed on excitation of the anterior roots of the 4th, 5th, 6th, and 7th lumbar segments agreed exactly with those obtained by Dr. **Risien Russell** ('Proc. Roy. Soc.,' vol. 54).

The results obtained by stimulating the central end of the posterior roots, which gave movement in the lower limb, are given below.

TABLE of Movements Obtained by Excitation of the Anterior and Posterior Roots in the Dog.

Dog.	FORGUE, p. 53. Anterior roots.	BERT and MARCACCI. Anterior roots.	Anterior roots.	Posterior roots.
1st lumbar	..	..	No movement in lower limb	No movement in lower limb.
2nd lumbar	..	..	No movement in lower limb	Slight flexion of hip and rarely flexion of knee.
3rd lumbar.	..	..	No movement in lower limb	Flexion of hip with adduction and rotation, and slight flexion of knee and of the toes.
4th lumbar.	Flexion of hip Adduction of thigh.	Flexion of hip	Slight extension of the hip Extension of the knee. „ „ ankle. „ „ toes.	Flexion of the hip. „ „ knee. „ „ ankle. „ „ toes.
5th lumbar.	Extension of knee with adduction.	Ext. of knee (BERT) „ hip (MARCACCI)	Extension of the hip with slight adduction. Extension of the knee. „ „ ankle. „ „ toes.	Flexion and adduction of the hip. „ of the knee. „ „ toes. Lateral flexion of the tail.
6th lumbar.	Femoral part of biceps producing ext. of knee with adduction.	Femoral part of biceps Producing ext. of knee.	Extension of the hip „ „ knee. „ „ ankle. „ with spreading out of the toes.	Slight flexion and adduction of hip. „ of the knee. „ „ ankle. „ „ toes. Lateral flexion of the tail.
7th lumbar.	“Fessiers” (?) hamstrings. Flexion of knee. Extension of thigh (p. 54). Extension ‘des orteils’ of big toes.	Flexion of knee Extension of thigh.	Extension of the hip. Usually „ „ knee. Occasionally flexion of the knee. Extension of the ankle. Usually extension with spreading out of toes. Occasionally flexion of the toes with or without spreading out. No movement in tail.	Slight flexion of the hip. „ „ knee. „ „ ankle. „ and occasional spreading out of the toes. Lateral flexion of the tail.
1st sacral	No movement in tail Action of peronei. Strong flexion of big toe.	Tail only	Slight extension of the hip Flexion of the knee. Extension with rotation out of the ankle. Usually flexion of the toes. Movement of base of tail and of the anal region.	Flexion of the knee. Extension (rarely flexion) of the ankle. Flexion of the toes. Movements in the tail, perineum, &c.
2nd sacral	Tail	..	No movement in lower limb Lateral movements in tail (specially the hip) and rectum.	Slight flexion of the knee and of the toes. Tail strongly, chiefly at the base and downwards protrusion of anus.

The great difference between these results and those obtained in the dog are that the diagrammatic contrast, so to speak, between the powerful extension at all joints of the lower limb obtained by stimulating the 5th, 6th, or 7th anterior lumbar root in the dog and the slower, yet marked, flexion at all joints obtained by stimulating the 5th, 6th, or 7th posterior lumbar roots in the dog is not obtained. In the monkey, results obtained by stimulating the *anterior* roots are complex, extension of some joints and flexion of others in varying degrees, both quantitative and qualitative, according to the root stimulated, being observed, and there is not the invariable extension characteristic of the dog.

The movements produced by stimulating the posterior roots are, of course, resultant effects, but with the exception of an occasional slight extension of the ankle or knee, according to the root stimulated, the main effect is that the bulk of the movement produced is that of flexion, in this case agreeing with that observed in the dog. Another interesting fact noted in the monkey was that, whereas by direct stimulation only the 3rd lumbar to the 1st sacral anterior root inclusive produces movement in the lower limb (RUSSELL, and the present experiments), direct stimulation of the posterior roots from the 12th dorsal to the 2nd sacral inclusive produced movement in the lower limb. From the latter fact it follows that the path for the sensori-motor reflex impulses in the cord must be both upwards and downwards, but this does not, of course, negative the general truth of the conclusion drawn from the experiments on the dog, namely, that for reasons (see above and below) the bulk of the impulses pass downwards.

A point arose in one experiment, which may seem to explain in part, or entirely, the difference in results obtained by previous observers, and notably that of SHERRINGTON and RUSSELL.

SHERRINGTON (*loc. cit.*) found that direct stimulation of the 2nd sacral anterior root produced movement in the toes; RUSSELL, on the other hand, proceeding with the greatest possible care and attention, failed in every instance to observe any movement in the lower limb under the same conditions. Stimulating in one case the 7th posterior lumbar root, I obtained movements as before described, but after gradually cutting the anterior roots from the 3rd lumbar downwards to the 1st sacral inclusive, all movement disappeared in the lower limb, though movements resulted in the tail and in the side in a most active manner, whereas, on performing the same experiment on the other (right) side, I was surprised to find that after section of the same anterior roots stimulation of the 7th posterior lumbar still evoked movement in the lower limb on that side, viz., slight extension of ankle, very slight flexion of the toes (as well as strong movement in the tail and in the side).

After careful investigation to see that no mistake had been made, I then cut through the right 2nd sacral anterior root, when neither from the 7th nor from any posterior root could I obtain movement in the lower limb. This seems to prove to me what one would expect on other grounds, viz., that the spinal cord in mammals is so complicated in structure and functions that slight varieties are to be expected in different members of the same series, or even, as in this case, there may be a difference in the two sides of the same body Of interest is the effect of dividing various roots and noticing the change in the resultant movement elicited by stimulating a certain posterior root. This could be done in so many ways and with so many nerve roots that it is not necessary here to give more than the general conclusions to which they lead. One or two experiments, however, may be of interest.

For instance, in one case stimulation of the 5th posterior lumbar root gave lateral movement of the side, contraction in the sartorius and hamstrings. The 5th anterior lumbar root was then divided, when from the posterior root, stimulated as before, movement in the gastrocnemius was added. That is, there ensued not only no diminution in the resultant movement, but a slight increase in another direction, as if part of the stimulus passing through the posterior root were prevented from passing out along all its normal paths, and, therefore, overflowed into another channel and gave an added effect.

The 4th lumbar anterior root was then divided in the same side, when, the 5th posterior root being stimulated as before, flexion of the side, contraction of the sartorius, and extension in the knee resulted, this last being an additional new movement.

Again, in another case, stimulation of the 7th posterior lumbar root gave flexion of the hip, slight extension of the knee, dorsal flexion of the foot, and inversion of the sole, whereas after division of the 7th anterior lumbar root excitation of the posterior root gave flexion of the hip, contraction of the hamstrings, extension of the knee, dorsal flexion of the ankle, strong flexion of the toes, and inversion of the sole, *i.e.*, again an addition of new movements.

Following this up, the 7th anterior lumbar root was next divided, after which stimulation of the 7th posterior root gave adduction of the hip, contraction of the hamstrings, extension of the ankle, flexion of the proximal joints of the toes, and extension of the distal joints, and movement in the side and tail.

After division, at intervals, of the 5th, 4th, and 3rd anterior lumbar roots no further difference in the movements resulting from stimulation of the 7th posterior root could be observed. But on dividing the 1st sacral anterior root, stimulation of the 7th posterior root gave only slight extension of the ankle, very slight flexion of toes, and movement in the tail and side, and finally, after dividing the 2nd sacral anterior root, excitation of the 7th posterior root evoked movement in the tail and side only.

Minute Localization within the Excitable Area.

In addition to the vertical distribution of the representation of movements in the lumbar enlargement (postero-external column) it was found that a minute differentiation could be made out in the lateral arrangement of the fibres in the column itself. Thus, in all the lumbar segments the following arrangement prevails :—

Repeatedly it was found that with a minimal stimulus it was possible to evoke movement either in the tail (and anus) only, or in the hamstrings, or in the hip, or in the side only, and whenever this was obtained, it was an invariable rule that the point for producing movement in the tail was placed in the cord mesially of that point stimulation of which gave movement in the hamstrings, and that this latter point was mesial of that for the hip, while most external of all was the point from which movement of the side of the trunk was elicited. Of course, if the strength of the stimulus were increased, then the current spread, and stimulating neighbouring points of excitability produced concurrent movement in two or more of above-mentioned parts, such as tail and knee.

This lateral arrangement has been in part foreshadowed by the observations of MOTT on the relation between the coccygeal nerves and GOLL'S column.

The movements resulting from excitation of a segment of the spinal cord in the lumbo-sacral region and those from excitation of the corresponding posterior root are similar, but are never quite identical. In each case flexion is the predominant effect, but in the former case the resulting movements are always stronger than in the latter, and frequently movements in other parts (tail, perineum, &c.) are added. This difference is to be expected, because, of course, in excitation of the postero-external column branches and fibres (ascending, descending, and collateral) many posterior roots are stimulated.

INVESTIGATION INTO THE SEGMENTAL REPRESENTATION OF THE CORD BY COMPARISON OF THE RESULTS OF EXCITATION OF THE ANTERIOR AND POSTERIOR ROOTS.

On pp. 199 and 201 is already given in tabular form the results obtained by different observers who have investigated this subject by stimulating the anterior roots.

The prevailing notion concerning the physiological function of representation of movement in the spinal cord is certainly that the fibres along which the stimulus passes when the posterior roots are excited, are short arc fibres, *i.e.*, limited horizontally to the segment they enter.

This simple view, however, is not borne out by the results of my experiments, as will be seen by the following account.

It was soon found that there were two sets of facts giving evidence of a different kind which showed (1) that the arrangement of the centres and their afferent fibres was more complex, and (2) that some change could be brought about within the centres by stimulation of the posterior roots which affected the excitability of the anterior roots.

(a.) *Character of Movement Elicited from the Respective Roots.*

There is a marked difference in the kind of contraction of the muscle, that from the anterior root being sharp, and that from the posterior root being more slowly developed.

(b.) *Kind of Movement Obtained from the Respective Roots.*

The most striking result, however, among these general considerations was the difference in effect obtained by excitation with the same stimulus, and under precisely the same conditions, and within a few seconds of each other, of the peripheral end of the anterior and the central end of the posterior root respectively.

It was then found that, whereas stimulation of the central end of the posterior root gave flexion of the whole limb, excitation of the peripheral end of the corresponding anterior root gave extension of the whole limb. Of course throughout these experiments there has been no excitation of the cerebral end of the anterior root, except when the nerve was stimulated in continuity. Besides the fact that the whole doctrine of recurrent sensibility, as originally formulated by **Majendie**, **Bernard**, and others, does not find much support at the present time, there is also the direct experimental evidence of **Gotch** and **Horsley** to show that stimulation of the cerebral end of the anterior root has no appreciable physiological effect on either the centres or channels in the spinal cord ('Phil. Trans.,' B, 1891), for these observers found that, whereas excitation of the central end of the posterior root gave maximal evidences of change in the electrical state of the spinal cord, on the other hand excitation of the central end of the anterior root not only produced no effect in the state of the spinal cord, but even stimulation of the central end of the whole of the anterior roots represented in the sciatic nerve gave, when the corresponding posterior roots were cut, no resulting change in the spinal cord whatever.

This remarkable functional distinction between the roots (viz., anterior, extension; posterior, flexion) was quite constant, and was obtained in every animal in which the experiment was made. Of course the movement which took place was a resultant effect, and was produced by the contraction of many muscles, each of which was concerned in producing either the flexion or extension of a particular joint, in one case acting with a combination of muscles when flexion resulted, and in the other case with another set of muscles when extension resulted. Hence stimulation of either of the anterior 5th, 6th, or 7th lumbar roots produces extension, and similarly that of the corresponding posterior roots flexion. So that in a sense the anterior and posterior roots appear to be antagonistic to one another in their action. Further, with spinal cord and nerves intact, stimulation of a posterior root (say the 5th) produces flexion of a joint, even when all the neighbouring anterior roots are divided. Hence this effect can only be due to the stimulus passing from the posterior root through the spinal cord along a particular anterior root to the muscles (differentiation of function in the nerve centres of that root), yet stimulation of this same anterior root produces extension. And this agrees entirely with the results obtained in a different way by Dr. **Risien Russell** ('Phil. Trans.,' B, 1893).

The above experiment also goes to show that stimulation of one posterior root causes impulses to pass out along many anterior roots.

For the particular function with which we are now concerned (sensori-motor reflex) it seems certain that the path along which the impulses pass, as evidenced by movement elicited in stimulating a certain posterior root, is directed towards a point below the level of that posterior root, and not, as we might suppose, chiefly in the same segment, or even above the level at which the posterior root joins the cord. The proof of this new conclusion is afforded by the following facts:—

Stimulation of the 3rd posterior lumbar root in the dog produces slow, but distinct, flexion and adduction of the hip and flexion of the knee; yet stimulation of the corresponding anterior or 3rd root, so far as I was able to observe in the thirty-five dogs experimented on, never produced movement in the lower limb; and this is all the more remarkable because a small branch is given off from the 3rd anterior root or nerve to the 4th anterior nerve, which latter supplies directly various muscles of the lower limb. Also stimulation of the 2nd anterior lumbar roots gave no movement in the lower limb, as one would expect; yet stimulation of the 2nd posterior lumbar root gave always distinct slight flexion of the hip and knee. Thus certainly for this segment it is clear that the posterior root is in relation with efferent paths at least two segments below its attachment to the cord.

Again, if, in stimulating any given posterior lumbar root, movement resulted in the lower limb, one or more of the anterior lumbar roots were then divided in various sequences, with the result that certain differences of movement could be observed. For instance, in one experiment excitation of the 6th posterior lumbar root gave flexion of the hip, knee, ankle, and toes, contraction of the dorsal muscles of the spine, and lateral movement in the tail to the same side; then, on dividing the anterior root of the 4th, of the 5th, and of the 6th lumbar nerves successively, the movements still obtained on the excitation of the 6th lumbar posterior root were apparently exactly the same as before the section of the anterior roots. The same fact was borne out by the following experiment in the opposite direction, viz., by dividing the roots from below upwards. In this experiment excitation of the 5th posterior lumbar root gave flexion of the hip, knee, ankle, and toes, and contraction of the dorsal muscles of the spine. The 1st sacral anterior root was then divided, and on stimulating the 5th posterior root as before the movements resulting were flexion of the hip and knee and dorsal muscles, but the flexion of the ankle was less than before, and the flexion of the toes was obliterated. The 7th anterior lumbar root was then divided, and the 5th posterior root stimulated as before, giving the result of flexion of the hip and the knee and of the dorsal muscles of the spine, but no movement in the ankle, or, of course, in the toes. In order to completely exclude the possibility of any efferent effects passing through the 2nd sacral—although my observations on the 2nd sacral anterior root accorded with those previously obtained by Dr. RUSSELL, showing that it has no functional relationship to the lower limb—it was next divided. The movement obtained by stimulating the 5th posterior still showed no change. The 6th anterior root was next divided. Excitation of the 5th posterior root, as before, now evolved only contraction in the back muscles and very slight flexion of the hip. The 5th anterior root was then divided, and stimulation of the 5th posterior lumbar root gave contraction in the back muscles as before, but no movement whatever in the lower limb. Of course, excitation of the 4th anterior lumbar root, on being stimulated directly, gave the ordinary result, viz., extension of the hip and knee, ankle, and toes, with spreading out of the latter.

By varying several other experiments of the same kind, precisely similar results were obtained.

From the foregoing results obtained by the excitation method, it may be justly concluded that the normal relationship of any given posterior root (sensori-motor reflex) to the segments in the spinal cord is that the destination of its root-fibres is nerve centres in segments below the point of entry into the spinal cord. It now remains to see how far this generalisation is justified by other facts obtained in other ways.

In the first place, the fact is of much interest that as long ago as 1847 CLAUDE BERNARD found that the 6th and 7th posterior lumbar roots supplied the 7th anterior root. Another point in the same direction is the fact that if the lumbar region be cut across, then stimulation of the posterior external column, as high as the margin of the cut surface of the lower portion, will give as intense a movement as before section.

Finally, the fact that all observers are agreed that, by the method of excitation of the anterior roots, the highest segment in the spinal cord from which movements have been elicited in the lower limb is the second. The experiments in the present investigation show that excitation of the cord as high as the 13th dorsal posterior segment evokes movements in the lower limb. This apparent discrepancy is, it will be seen, a proof of the position just advanced, since it shows that the uppermost nerve centre containing motor representation of the lower limb received afferent impulses by means of the posterior root, which is two or three segments higher (nearer the cerebrum). Evidence of a like kind is afforded by anatomical researches.

In the first place, SCHULTZE found that after damage to the cervical enlargement a comma-shaped area of descending degeneration occurred in the posterior columns. BARBACCI found also after a transverse lesion of the cord that scattered descending degeneration could be found throughout the whole breadth of the posterior column.

The most important anatomical fact, however, is the well-known discovery by RAMON-Y-CAJAL, confirmed by KÖLLIKER, RETZIUS, and GOLGI, that the posterior root fibres divide almost immediately upon their entrance into the cord into two main branches, one ascending and one descending. I venture to provisionally suggest that the ascending branch is, perhaps, chiefly concerned with sensory (*i.e.*, cerebral) impulses, and the lower branch with local sensori-motor reflex actions.

It has also been shown in the horse that there is a difference in level between the sensory and motor nerves which supply the sternomastoid muscle, the sensory nerve being two or three segments higher. It is very noteworthy also that the same antero-posterior relationship of sensory and motor nerves also prevails largely in the cranial nerves.

SUMMARY AND CONCLUSION.

1. *Relationship of Posterior Roots to Reflex Kinæsthetic Centres.*

It appears from the foregoing experiments to be definitely established that any reflex centre derives its chief afferent impulses from a nerve root which enters the cord as a rule about two segments higher, *i.e.*, on the cephalic side.

This generalisation, established by the method of excitation, is confirmed by anatomical and pathological observations.

2. *Lateral Arrangement of Fibres in* BURDACH'S *Column.*

The fibres of the postero-external column are arranged in a definite and constant order from within outward, the innermost fibres (*i.e.*, those nearest the middle line) representing the most distal portions of the tail and lower limb, and the outermost the proximal.

3. Whereas direct excitation of the anterior roots in the dog produces as a resultant movement extension of the lower limb, the resultant movement produced from the reflex kinæsthetic centres of excitation of the posterior roots is always flexion. In the monkey there is not this apparent antagonism, because stimulation of the anterior roots in that animal brings out a differentiation of flexion and extension, although excitation of the posterior root gives flexion alone.

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the evidence which I will bring forward tends to show that the tract which I am about to describe is part of this system: I shall therefore, to avoid confusion, term it the *upper decussation of* **Forel.** Care must also be taken not to confound it with **Meynert's** commissure.

By a limited section passing through a portion of the thalamencephalon D. and P. succeeded, in the new-born cat, in producing atrophy of one decussating tract. They concluded that the "Forel'sche Kreuzung ist ein vollkommen selbständiges Fasersystem, und hat mit der sogen: Meynert'schen Commissur nichts gemein. Die Fasern der Forel'schen Kreuzung stellen einen Theil desjenigen Fasersystems dar, welches nach vorn (Cerebralwärts) vom rothen Kern der Haube liegt, ventralwärts verläuft, sich unterhalb des 3. Ventrikels kreuzt, hierauf längs der ventralen Fläche des Hirnschenkels zwischen diesem und den Tractus opticus weitergeht und den Nucleus Lenticularis an seiner basalen Seite erreicht."

The following illustrations, figs. 1, 2, and 3, are taken from cats in which a hemisection was made through the mesencephalon, passing through the posterior margin of the superior corpus quadrigeminum and the third nerve of the left side, and extending upwards in one case into the thalamus. They show a well-marked group of large degenerated fibres, which sweep round the third ventricle in front, arising in the thalamic area of the one side, and extending far into the internal capsule of the other. These fibres coincide in many ways with D. and P.'s description of **Forel's** commissure.

In a section of the mesencephalon in the region of the wound, and through the nuclei of the IIIrd nerve, large fibres pass in a curved sweep from the injured side forward across the IIIrd nerve and raphe, towards the anterior portion of the IIIrd nerve of the opposite side. Having reached the anterior and inner aspect of the red nucleus, the majority of the fibres at this level turn directly downwards, and give origin to the lateral tract of the cord, as described in my first paper.* This crossing I have assumed to represent **Forel's** fountain decussation. I will now, for reasons given above, term it the *lower decussation of* **Forel.** The fibres originate in the posterior tegmental gray matter. In a section immediately above the origin of the IIIrd nerves very distinctly degenerate fibres are seen crossing the raphe from the side of the lesion. These fibres are not so numerous or so closely bound together as in the "fountain" decussations of **Forel** and of **Meynert**, but their position and their very characteristic large size point to a very close relationship to these decussating systems (fig. 1).

Proceeding upwards through the sub-thalamic area and region of the third ventricle, degenerate fibres can be traced lying scattered in the tegmentum between the superior fillet and the pes pedunculi. At a little higher level, namely, at about that of the anterior third of the thalamus, the fibres bend horizontally and pass forward in a loose bundle between the fornix and the third ventricle. More anteriorly they collect into a well-marked bundle, and sweep round the anterior extremity of the third ventricle. In this position the fibres are readily distinguished from those of MEYNERT'S commissure; they are very large in size, whilst MEYNERT'S fibres are very small. Having passed the ventricle the fibres again diverge slightly, and pass backwards to the neighbourhood of the optic tract lying between it and the fornix. The degenerate fibres thus lie on the side of the lesion internal to the fornix, whilst on the opposite side they are external. As they proceed backwards the fibres are again grouped closely together, and lie as a compact bundle between the internal capsule (pes pedunculi) and the optic tract. Still further back they arch inwards into the internal capsule, thus avoiding the globus pallidus, and appear to lose themselves in the outer area of the thalamus (fig. 2).

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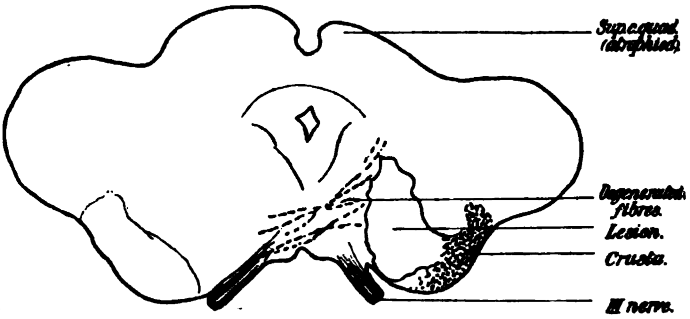
* 'Proc. Roy. Soc.,' 1894 (Abstract), see fig. 1.

Fig. 1.



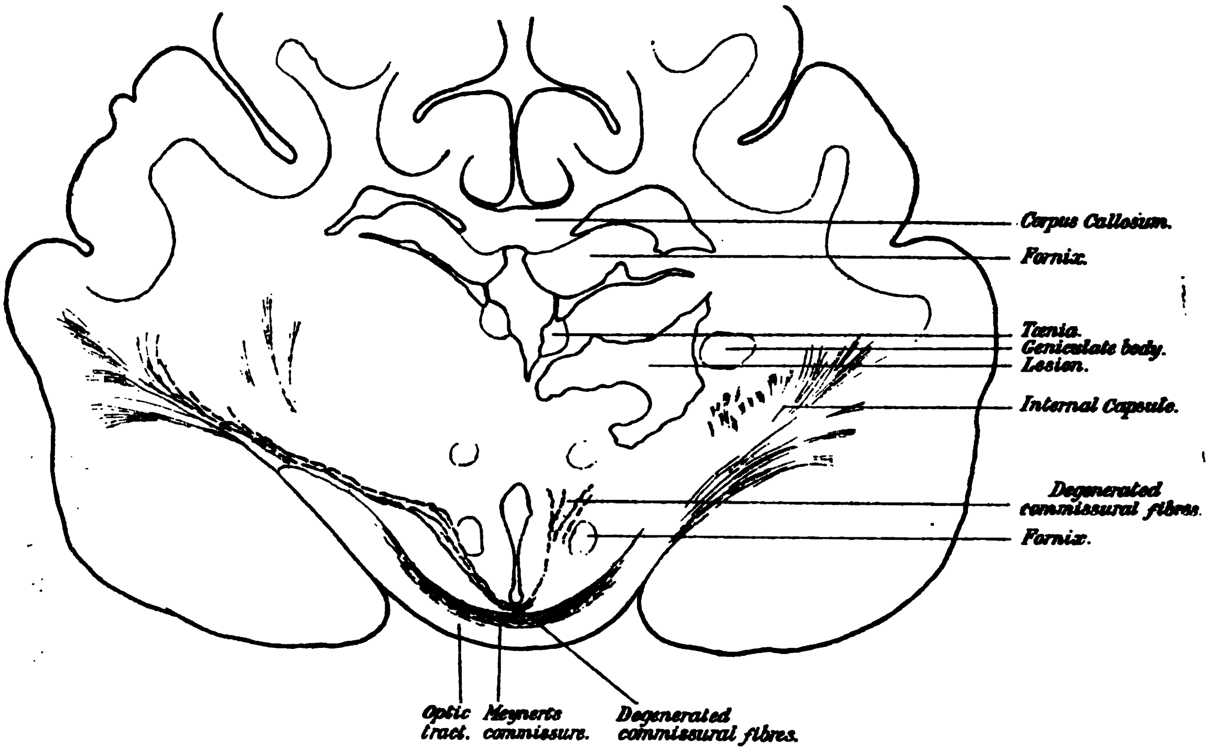
Section through the mesencephalon and the centre of the superior corpora quadrigemina to show decussating degenerate fibres, FOREL'S decussation. All figures magnified three times, lesion on left side. Drawn with projection apparatus.

I have not been able to trace the fibres to a more definite ending, and although they at one time appear as if they would continue side by side with the capsular fibres to the cortex, yet careful examination fails to show this.

The description given above coincides in very many details with that given by DARKSCHEWITSCH; the method of MARCHI has, however, enabled me to show that the degeneration proceeds from the tegmental area at the level of the lesion, gradually extends upwards and forwards, curves round to the opposite side, and appears to end in the lateral thalamic region (or possibly cortex), and not in the lenticular nucleus.

The interest of this tract is its undoubted close connexion with the arcuate system of fibres of the lower mesencephalon and probably of the bulbar segments. In my previous paper I drew attention to the relationships of MEYNERT'S and FOREL'S fountain decussations to one another. It was shown that the one formed the antero-lateral column, the other the lateral, there being a gradual transition from the one to the other. MEYNERT'S decussation extended further caudally; FOREL'S, on the other hand, ceased earlier and extended higher up (cerebrally). Both decussations are especially well marked in the lower animals, and both are conspicuous by the largeness of the medullary sheath, and in consequence by the striking osmic acid reaction of degeneration. The fibres of FOREL's fountain decussation I could never trace to a definite focus, they arise in the lateral tegmental area on each side of the Sylvian gray matter, and they terminate in the lateral column of the cord. The fibres described above likewise arise in the lateral tegmental area, are of the same size, arch round in front of the continuation of the aqueduct of Sylvius, viz., the third ventricle, and appear to end in the lateral thalamic region. There is no marked gap between this upper decussation of FOREL and the lower one, scattered degenerate decussating fibres binding the two together. I therefore conclude that these fibres are homologous to the arcuate fibres of lower segments. They take origin at a slightly higher level than the fibres of the lower decussation, but it is a very striking fact that they then gradually *ascend* to their termination. There is, in fact, a fan-shaped system of decussating fibres, which arises in the tegmentum, extending the length of the superior corpus quadrigeminum and lower part of the thalamus; from this basis the fibres spread out slightly upwards and downwards, the latter turning

Fig. 2.



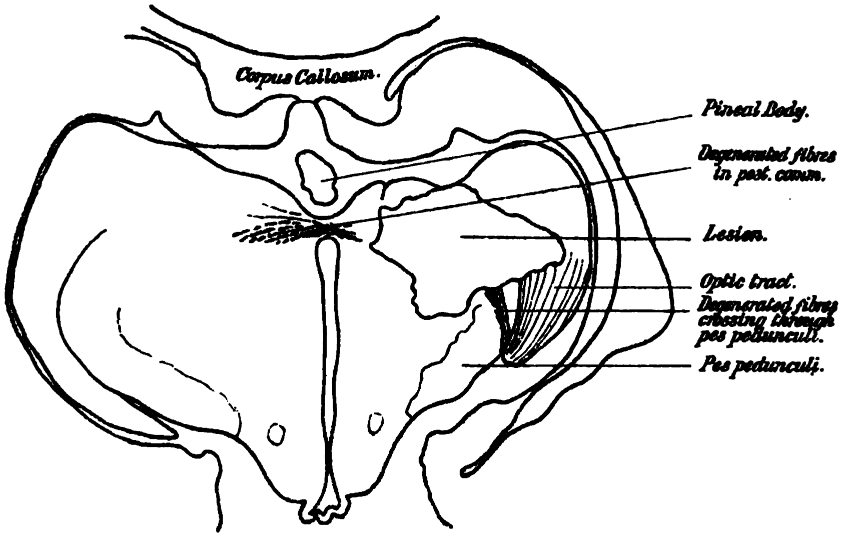
Frontal section through the internal capsule and optic chiasma. A lesion is shown on the right side, causing extensive destruction of the thalamus. In the sub-thalamic region large degenerate fibres group themselves into a commissure, which passes in front of the ventricle and proceeds to the opposite side, where it loses itself in the internal capsule close to the cortex.

directly downwards after they have passed out a certain distance. From this region in the mesencephalon the degeneration is centrifugal.

Meynert's Commissure.

This commissure enters into the formation of the schema of the fillet described by **Bechterew**.* He states that the fillet fibres are not only connected with the globus pallidus of the same side, but by means of **Meynert's** commissure are brought into relationship with that of the opposite side. The latter commissure also serves to bind together the lenticular nucleus and the corpus Luysii; he thinks that **Darkschewitsch** and **Pribytkow** (*l.c.*) have disproved the view that it connects the two corpora geniculata interna. These last authors describe the connexion of the tract with the stalk of the nucleus lenticularis, there mixing with the fibres which surround the basal surface of the lenticular body. In addition they describe a not inconsiderable bundle of fibres which does not reach the lenticular nucleus, but which arches inwards transversely across the dorsal portion of the pes pedunculi and enters the corpus Luysii. Not all the fibres, however, enter this body, a few passing back dorsally to penetrate the region of the thalamus, to intermingle with the fibres of the upper (median) fillet.

Fig. 3.


Corpus Callosum.
Pineal Body.
Degenerated fibres in post. comm.
Lesion.
Optic tract.
Degenerated fibres crossing through pes pedunculi.
Pes pedunculi.

Section through the interbrain close to the mesencephalon, and passing through the posterior-commissure. The lesion involves the thalamic region, corpora geniculata, commencement of superior corpus quadrigeminum, and portion of the pes pedunculi. Degenerated fibres are seen in the posterior commissure, and a tract of them crossing the pes pedunculi.

In my own experiments I have succeeded in producing degeneration of a tract

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* *Loc. cit.*

(figs. 2 and 3), which may correspond to **Meynert's**; nevertheless, I have found it impossible to come to a definite conclusion as to its complete mode of origin and termination.

Fig. 3 is a section made through the lower caudal portion of the thalamic region, and shows the original wound caused by the hemisection. A group of degenerate fibres arches through the pes pedunculi, springing from the region of the corpus Luysii and the region immediately posterior to it, both of which are involved in the lesion. The degenerate fibres group themselves into a well-marked bundle closely applied to the outer aspect of the pes pedunculi and between it and the optic tract. The fibres then pass anteriorly with the optic tract and cross in front of the 3rd ventricle, as seen in fig. 2. They then turn back and caudally along the inner side of the optic tract. As they descend caudally they appear to diminish in number, and not to enter the corpus Luysii of the sound side; a few of the fibres may penetrate with the optic tract into the thalamic region and intermingle with the superficial fibres of the superior fillet. In the same section, owing to the extension upwards of the wound, the ansa lenticularis was very completely degenerate; notwithstanding this I could trace no actual connexion between these degenerate fibres and **Meynert's** commissure. From an examination of a large number of sections it would appear that **Meynert's** commissure has a wide seat of origin, numerous fibres either passing through, or arching round, the pes pedunculi on its dorsal aspect to form it. The latter fibres may be upper fillet fibres coming from the superior corpus quadrigeminum.

The Posterior Commissure.

The posterior commissure is usually divided into dorsal and ventral fibres. **Darkschewitsch** traces fibres from the ventral portion into the posterior longitudinal bundle and to a close relationship with the root of the third nerve. **Bechterew** states that he finds that in the Mole the fibres of the posterior longitudinal bundle end in the upper oculomotor nucleus, and that in the same animal the ventral portion of the posterior commissure is of considerable size. **Held*** figures fibres crossing in the commissure and turning down in the anterior lateral column system of the opposite side. I have had the opportunity of examining this commissure in numerous cases of unilateral lesion extending along the region of the superior corpus quadrigeminum.

In fig. 3 the edge of the wound abuts directly on the posterior commissure and extends for a considerable distance both above and below the commissure. The extent of the lesion downwards is well seen in the next figure (fig. 4), taken through the inferior corpus quadrigeminum. There was no doubt, therefore, that in this case the fibres which entered the commissure from one side were very completely interrupted. An examination of a series of sections shows that the degenerate fibres resulting from the lesion have not a long course. In the first place, the fibres do not, as a rule, run horizontally across the commissure, but arch obliquely. They are most conspicuous in the ventral portion of the commissure, and a large number of them terminate in the dorsal and opposite lateral aspect of the Sylvian gray matter, a few scattered fibres appear to curve round the gray matter and to extend towards the raphe, but I have not been able in any instance to trace degenerate fibres into the posterior longitudinal bundle. Other fibres radiate into the posterior tegmental area, and the remainder into the corpus quadrigeminum. The fibres which cross, therefore, in the posterior commissure appear to have a short course, they focus in the central and ventral aspect of the commissure and then diverge again, there is thus an interlacement in the commissure. There are few fibres in the dorsal portion of the commissure. When the preceding commissure is compared with that forming the roof of the aqueduct lower down, differences become apparent. Fig. 4 is a section passing through the posterior corpora quadrigemina. It will be seen that the commissural system is much more extensive than higher up, and that the fibres for the most part run straight across and then spread out in the opposite corpus quadrigeminum. There is no ventral concentration of fibres, the commissure being uniform throughout; the fibres are slightly smaller than those in the posterior commissure. I have not succeeded in tracing any around the Sylvian gray matter, the fibres appearing to terminate in the corpus quadrigeminum. In addition to the above system of fibres, there are large medullated fibres, which for the most part lie superficially in the roof, and they appear to terminate in the lower portion of the superior or upper portion of the inferior corpus quadrigeminum. Their origin will be discussed immediately.

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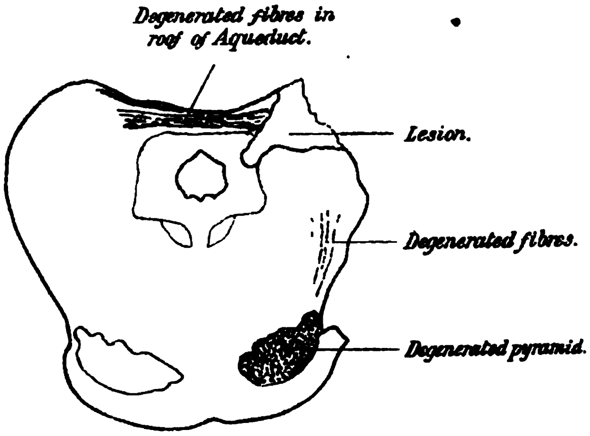
* **Held**, "Die Centrale Gehörleitung," 'Archiv f. Anat. u. Phys.,' 1893.

Fig. 4



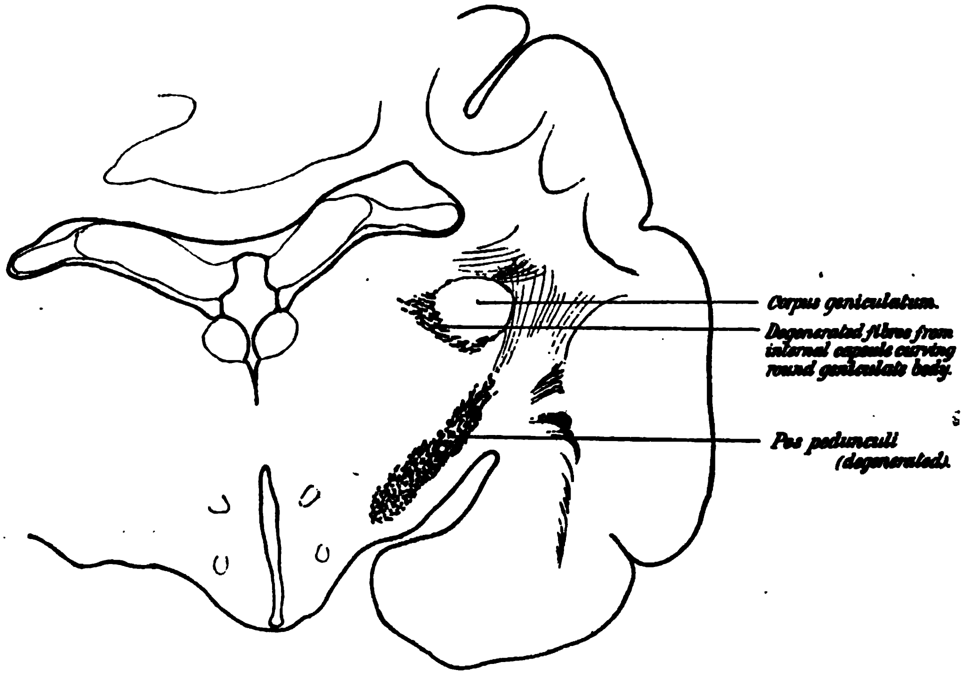
Section through upper part of pons and inferior corpora quadrigemina, to show degenerated fibres passing back from the pyramid to the quadrigeminal region, also degenerated fibres in the roof of the aqueduct.

In conclusion, it may be stated that the degenerate fibres, which cross in the commissure or roof of the aqueduct, and which result from a unilateral lesion of the quadrigeminal area, have not a long course, but terminate for the most part in the opposite corpora quadrigemina, dorsal and lateral aspects of the Sylvian gray matter, or posterior portion of the tegmentum.

The Dorsal Fibres of the Commissure in the Roof of the Aqueduct of Sylvius.

I first noticed the degeneration of these fibres in cases where the anterior third of one cerebral hemisphere had been removed, and in which, therefore, there was very complete degeneration of the internal capsule. Sections through the middle region of the thalamus clearly showed a group of scattered large degenerate fibres leaving the internal capsule and entering the optic thalamus. The fibres (fig. 5) pass downwards and inwards; they encircle the median geniculate body, and then turn upwards, passing beneath the fibres going to form the optic tract, as well as the corpora geniculata and pulvinar. They become superficial in the stalk of the superior corpus quadrigeminum, lying in the rear, between the pulvinar and the corpus quadrigeminum (figs. 6, 7). They penetrate the corpus, many of the fibres probably terminating here; others, however, remain or become superficial in the hinder portion of the superior corpus, and cross over to the opposite side in the roof of the aqueduct of Sylvius as the large medullated fibres described above. The fibres are not traceable below the inferior corpus, and they appear to remain confined to the quadrigeminal bodies.

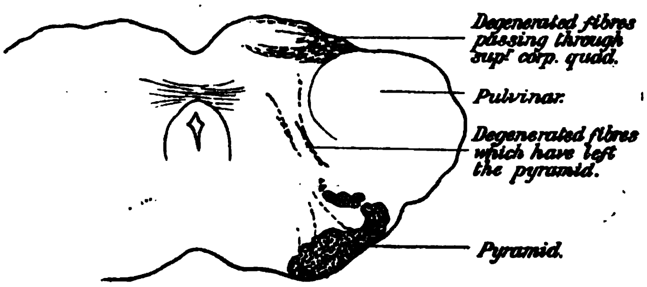
Fig. 5.


Corpus geniculatum.
Degenerated fibres from internal capsule curving round geniculate body.
Pes pedunculi (degenerated).

Frontal section through brain, behind level of fig. 2. Cat, anterior $\frac{1}{3}$ of left hemisphere removed.

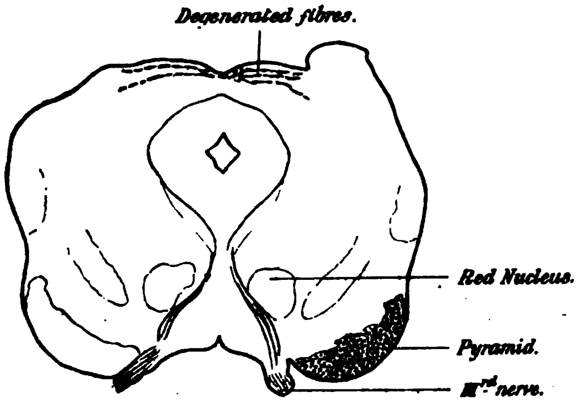
There is not yet sufficient evidence to say whether these fibres are of cortical origin, but appearances would favour the view. The fact remains, however, that a descending tract of fibres leaves the internal capsule, traverses the thalamus, and is distributed to the quadrigeminal region of the opposite, and probably of the same, side. The reason for supposing the fibres to be of cortical origin will appear more clearly in the next section, where it will be shown that fibres leave the pes pedunculi and pass backwards to the quadrigeminal region.

Fig. 6.


Degenerated fibres passing through supr corp. quad.
Pulvinar.
Degenerated fibres which have left the pyramid.
Pyramid.

Section through mesencephalon above the level of the IIIrd nerve, to show fibres derived from internal capsule and pyramid.

Fig. 7.



Section through mesencephalon, red nuclei and 3rd nerves, to show termination of degenerate fibres which have come from the internal capsule.

II.—The Pyramidal System in the Mesencephalon and Bulb.

An examination of consecutive series of sections of a large number of cases of pyramidal degeneration in the cat, showed unmistakably that degenerate medullated fibres leave the pyramidal system in the mesencephalon, pons, and medulla. At first, owing to their fewness in number, their presence was regarded as accidental; careful examination, however, revealed them in all cases, and, moreover, in a recent paper **Muratoff*** has figured them in two situations in the bulbar segments.

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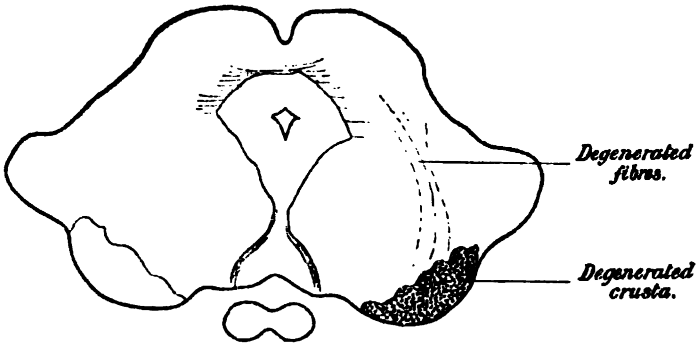
* Muratoff, 'Archiv f. Anat. u. Phys.,' 1893; and recently Rothman, 'Neurologisches Centrlb.,' June, 1896.

The fibres turn horizontally out of the pyramid and pass backwards, usually across the raphe, to the opposite side. They cannot be traced by this method to end in the motor nuclei; all that can be said, is that they lose themselves in the hinder portions of the tegmentum.

Mesencephalon.—Small groups of fibres were found to leave the dorsal and inner portion of the pes pedunculi (fig. 6), and to pass backwards to the tegmental, commissural region of the same side, but whether they actually crossed over in the posterior commissure to the opposite side is not proved. In fig. 6 the relationship of these small bundles to the fibres derived from the internal capsule is well seen, and makes it probable that the latter are also of cortical origin.

Fig. 8 shows degenerate fibres leaving the *crusta* further down to pass back to the quadrigeminal region of the same side. These fibres appear to be fairly numerous, and MURATOFF (*l.c.*) has drawn attention to them.

Fig. 8.



Section through mesencephalon at upper limit of IIIrd nerves and superior corpora quadrigemina, to show degenerated fibres leaving the degenerate crusta and passing back to the quadrigeminal region.

Pons.—There is every reason for supposing that the pyramidal fibres undergo diminution in this region. Their mode of termination is very obscure, however, and only a few fibres turn horizontally out to cross the raphe, and end in the tegmentum of the opposite side.

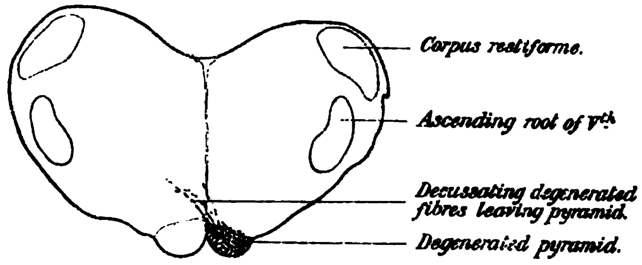
Medulla.—A considerable number of fibres may be observed leaving the inner angle of the pyramid in the upper portion of the medulla, corresponding to the region of the nucleus of the Vth. The fibres cross the raphe, and end in the tegmentum in the vicinity of the direct lateral columnar fibres.

Corresponding to the nuclear areas of the VIth and VIIth nerves, a number of fibres also leave the inner part of the pyramid (fig. 9). Attention has again been directed to them by MURATOFF (*l.c.*), who supposes that they are the cortical motor fibres of the VIIth. I have not observed them terminating in the nucleus, but I have seen them terminating close to the nucleus of the VIth.

Just below the level of the trunk of the VIth nerve fibres may be seen leaving the inner angle and dorsal aspect of the pyramid, to disappear at the dorsal aspect of the nucleus lateralis of the opposite side.

At levels corresponding to the area of the hypoglossal nucleus, fibres are given off from the inner posterior and inner anterior corners of the pyramid; the latter traverse the sound pyramid of the opposite side. The fibres run backwards and to the opposite side in the bundles of sensory decussating fibres. They appear to end in the tegmental region external to the nucleus of the XIIth.

Fig. 9.



Section through the mid medullary region a little below exit of VIIth.

Still lower down, at the lower end of the medulla, both pyramids sink deeply towards the central canal; previous to decussation, however, numerous fibres cross to the opposite side in the bundle of the sensory decussation, and with the latter fibres they lose themselves in the hinder tegmental region.

It seems very probable that the fibres described above serve to connect the pyramidal system with the motor centres of the quadrigeminal region and bulb. The decussation of the pyramid is thus not confined to the upper cervical region, but, as one would expect, is gradually taking place during the descent of the pyramid through the bulbar segments. As has already been seen, the majority of the fibres decussate; a few, however, and this is notably the case in the quadrigeminal region, appear to remain on the same side. This again accords with the fact that there are also direct and crossed paths to the motor centres of the cord.

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Horsley, Victor, and Kramer, S. P.—On the Effects produced on the Circulation and Respiration by Gun-shot Injuries of the Cerebral Hemispheres.
Phil. Trans., B, 1897, vol. 188, pp. 223–256.

Brain, Effects on Circulation and Respiration produced by Gun-shot Injuries of Hemispheres—causation and mode of production of same.
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Kramer, S. P., and Horsley, Victor.
Phil. Trans., B, 1897, vol. 188, pp. 223–256.

Gun-shot Injuries of Cerebral Hemispheres, Effects on Circulation, Respiration, &c.—destructive effects on Encephalon.
Kramer, S. P., and Horsley, Victor.
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Muscular system, excitation by passage of Bullet through Cerebral Hemispheres.
Kramer, S. P., and Horsley, Victor.
Phil. Trans., B, 1897, vol. 188, pp. 223–256.

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the injury. We have, however, collected from the literature of gun-shot injuries such facts as receive general acceptation at the present day: and, further, have arranged together the results of previous experiments by various investigators who have thrown light on the causation and mode of production of the destructive effects exerted by bullets on solid bodies and animal tissues.

SEYDEL ('Lehrbuch der Kriegs-Chirurgie,' Stuttgart, 1893) states, p. 20, that in the general shock immediately following the infliction of any severe gun-shot wound there are, so far as the pulse and respiration are concerned, the following changes: "The pulse is small, often scarcely perceptible, very frequent, and easily compressible. The respiration is accelerated and very superficial."

In speaking of the symptoms due to local injury (p. 142), he re-states these changes without alteration, except in cases where a general increase of intra-cranial pressure occurs as a result of hemorrhage into the skull cavity.

McCORMAC attributes the symptoms of gun-shot injury of the brain to the compression brought about by hemorrhage. In cases where there is direct injury to the medulla oblongata, he states that that is accompanied by the occurrence of CHEYNE STOKES' respiration and a slow pulse. (Article "Gun-Shot Wounds," 'HEATH's Dictionary of Practical Surgery,' 1887.)

The history of the experiments which have elucidated the physical conditions produced in substances of varying density is given in an Appendix, see p. 252, and wherever any special point is discussed in the paper.

METHOD OF INVESTIGATION.

Anæsthetic.—The anæsthetic we have invariably employed has been ether administered by a funnel attached to the tracheotomy tube. The anæsthetic was removed just before the moment of firing the shot, so as to avoid error arising from an excess of the drug.

Record of the Circulation.—The movements of the heart and the pressure of the blood were recorded by means of an ordinary mercurial manometer, the cannula being placed in the femoral artery, or, more rarely, in the carotid. Care was taken only to employ one carotid in any one experiment, so as to avoid the interference (HURTHLE), however slight, which ligature of the two vessels brings about.

In certain cases the cannula was placed in the peripheral as well as in the central end of the artery, with the object of comparing, as far as possible, the effects due to the vaso-motor system as distinct from the alterations in pressure produced by the heart.

Record of the Respiratory Movements was obtained by means of a Paul Bert exploring tambour applied to the thorax of the animal by a strap passing round it and attached to each end of the tambour. This apparatus consequently records only the movements of the expansion and contraction of the whole chest.

Record of Movements.—At the moment of penetration by the bullet there ensued definite motor phenomena, which we were able to record. Thus, the muscles contracted powerfully and then relaxed. This was graphically recorded by attaching the rectus femoris muscle to a Fick spring myograph.

Record of the Changes in the Intra-cranial Tension.—To record changes in the intra-cranial tension, a steel tube, 1 centim. in diameter, was screwed and fixed by a vice immovably in a trephine hole, filled with ·6 per cent. NaCl solution, and then connected by a rubber tube with a writing tambour.

For purposes of direct observation of the pressure upon and dislocation of the brain an opening was sometimes made in the postero-parietal region, and the dura mater divided.

Record of the Moment of Firing.—To obtain this, the following expedient (Woolwich method) was resorted to:—Across the muzzle of the rifle or pistol was stretched a very fine brass wire, which the bullet divided in its course, and the rupture of which caused an electric signal to mark on the paper.

Record of Time.—The time was recorded in the experiments with accuracy by a metronome beating seconds, and transmitting its rhythm by an electric signal to the kymographic paper.

Rifles Employed.—We have used the following arms to obtain our results:—

(*a.*) Rook rifle . ·38 calibre, short cartridge, conico-cylindrical bullet.
(*b.*) „ „ . ·22 „ „ „ „ „ „
(*c.*) Saloon pistol ·22 „ cylindrical bullet, with hemi-spherical ends.

In fig. 1 (Plate 3) are shown the cartridges and bullets of the natural size. The muzzle velocities of the rifles and pistol were very kindly measured for us by Mr. H. T. Ashton, at the Royal Laboratory Velocity Range, Woolwich, by direction of Dr. Anderson, who most courteously gave us every assistance. To Mr. Ashton we are indebted for the following figures, which are derived from the observed velocities (distance of screen noted below), according to Bashforth's tables for ogival-headed projectiles:—

(*a.*) Rifle . . . ·38 calibre (60 ft. 0 in. screen used.) Mean of three observations: muzzle velocity, 970 feet per sec.
(*b.*) „ . . . ·22 „ (60 ft. 0 in. screen used). Short cartridge. Mean of four observations: muzzle velocity, 1029 feet per sec.
(*b′.*) „ . . . ·22 „ (90 ft. 0 in. screen used). Long cartridge.* Mean of three observations: muzzle velocity, 1076 feet per sec.
(*c.*) Saloon pistol ·22 „ (60 ft. 0 in. screen used.) Mean of five observations: muzzle velocity, 646 feet per sec.

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* Used very rarely. See list of *post mortem* examinations at the end of the paper.

Ammunition Employed.

The following table shows the composition of the cartridges used :—

	Weight of powder.	Weight of bullet.
	gramme.	grammes.
(*a*.) ·38 calibre, Short cartridge, ELEY's manufacture	·68	8·05
(*b*.) ·22 ,, ,, ,, Rifle, American manufacture . . .	·17	1·87
(*c*.) ·22 ,, Saloon pistol, ELEY's manufacture	·07	·97

In (*c*) the finest sporting powder was used. The remarkable excellence of ELEY's ammunition and accuracy of filling, &c., was strikingly borne out by the great constancy in the muzzle velocity obtained with ammunition (*a*).

RESULTS OF THE PRESENT INVESTIGATION.

We will discuss the effects observed according as they relate to the following systems :—

A. Respiratory.

B. Cardiac. $\left\{\begin{matrix}\text{Rhythm}\\ \text{Force}\end{matrix}\right\}$ of the heart beat.

C. Vasomotor.

D. Muscular.

A. *Effect upon the Respiratory System.*

(1.) *Phenomena observed at the Moment of Shot.*

The effect produced upon the respiratory movements was invariably the same in all cases in which the skull was intact, and in which the bullet penetrated the brain with moderate velocity. The effect was sudden and complete arrest of the respiratory movement (see fig. 5, *et seq.*). The immediate effect of the passage of the bullet through the hemisphere was almost invariably a very marked and sudden inspiratory spasm.

In a few instances there was noted expiratory spasm. In a smaller proportion still the respirations simply ceased, the chest assuming a midway position.

This arrest was in practically all cases permanent unless artificial respiration was commenced, when in a certain number of cases the respiratory movements could be re-established (*vide infra*).

In all tracings of the arrest it will be seen that the chest ultimately assumed a position of equilibrium, probably by relaxation of the tone of the respiratory muscles.

Under these circumstances the recording lever reached a point midway between the inspiratory and expiratory apices of the curve taken before the shot.

(2.) *Mode of Recovery of Respiratory Movements.*

(*a.*) Spontaneous.

(*b.*) After artificial respiration has been established.

(*a.*) *Spontaneous Recovery of Respiration.*—This event (very rare with the skull intact, that is, not opened previous to the shot) (see p. 242) presented itself in one case, in which the bullet traversed the frontal lobes near the base midway between the optic chiasma and the anterior pole of the hemisphere, and is interesting because the arrest of the respiration by the shot was followed by a period of asphyxia of such length as to nearly reach the physiological limit usually assigned, viz., of four minutes. The recovery of respiration was exactly the same as that described under (*b*). The full discussion of this important point will therefore with advantage be postponed.

(*b.*) *Recovery after Artificial Respiration.*—Recognising from the first the fatal character of the arrest of the respiration, we instituted artificial respiration a few (10 to 30) seconds after the shot, and found that the respiratory movements could be restored except under circumstances to be alluded to directly. When recovery occurred it presented the following characteristics. The respiration returned by small inspirations, usually at long intervals. Very often these inspirations were of a sighing character, and consequently the tracings frequently exhibited two or three apices on each respiratory movement. The movements gradually deepened in extent and increased in frequency.

If the recovery took place during the execution of artificial respiration, the natural respiratory movements occurred between the artificial ones.

Very commonly at the commencement of the recovery, and occasionally also as the respiratory centre died, the phenomenon of shallow respirations alternating with deep ones was observed.

After the fact of variability in depth, alteration in regularity of the rhythm is the next most important factor. This was well exemplified in Experiments 9, 22, 32, where it was seen that both the recovery and failure of the respiratory centre was accompanied by great irregularity in the rhythm of its discharge.

That the recovery of the respiratory centre is complete under the circumstances just detailed, was tested by us in two ways, (1) by inducing asphyxia, (2) by dividing the vagi.

(1.) Upon clamping the trachea the expiratory convulsive respiratory movements which followed were in every respect characteristic of the usual disturbance of the respiratory centre effected by asphyxia.

(2.) Division of the vagi called forth the typical deep inspiration, the prolonged pause, and the collapsing expiration, characteristic of the section of these nerves.

B. *Effect upon the Heart Beat.*

The prevailing opinion among clinicians, that the chief pathological effect of the passage of a bullet through the cerebral hemisphere is exerted upon the heart, is, as we have already stated, not borne out by the exacter methods of experiment.

The effects actually noted by us are best described under the headings of

(*a.*) Rhythm,
(*b.*) Force,

and must be further arranged as primary and secondary according as to whether the effect is produced at the moment of the shot by virtue of the passage of the missile within the skull, or whether it is due to rise of the intra-cranial tension in consequence of hemorrhage, &c. We will reserve the discussion of the changes in blood pressure until we discuss the vasomotor phenomena under Part C.

Primary Effects.

(*a.*) *Rhythm.*—The passage of the bullet through the hemisphere has either no influence, or produces a very slight effect upon the heart rate.

Thus of 59 observations the rate was absolutely unaltered in 26 instances; very slightly slowed (7·5 beats in a minute) in 4 cases; slightly slowed, *i.e.*, a diminution of from 15 to 45 beats per minute, in 18; and in 11 slightly accelerated.

From these facts it is obvious that the cardio-vasal nerve centres are unlike the respiratory centre, in that they are not so notably influenced by the presence of the bullet.

Where change occurs in the heart rate it appears to be the result of an excitation, chiefly of the vagal centre. We shall further discuss this matter in considering the secondary effects.

(*b.*) *Force.* The force of the heart beat at the moment of the shot was roughly estimated by the excursions of the manometer, and as will doubtless be anticipated, in a very large majority of cases, did not show any material alteration. Thus, of the 59 experiments above quoted, in no less than 43 the force of the heart beat was unchanged, while in seven it was very slightly diminished, and in only two instances considerably so; these last being cases where the ·38 cal. rifle was employed. In seven experiments the force was slightly increased. Thus, on the whole the action of the heart seemed to be scarcely affected at the moment when the bullet traversed the hemisphere (see, however, also the discussion of the changes in the blood pressure on p. 231, *et seq.*).

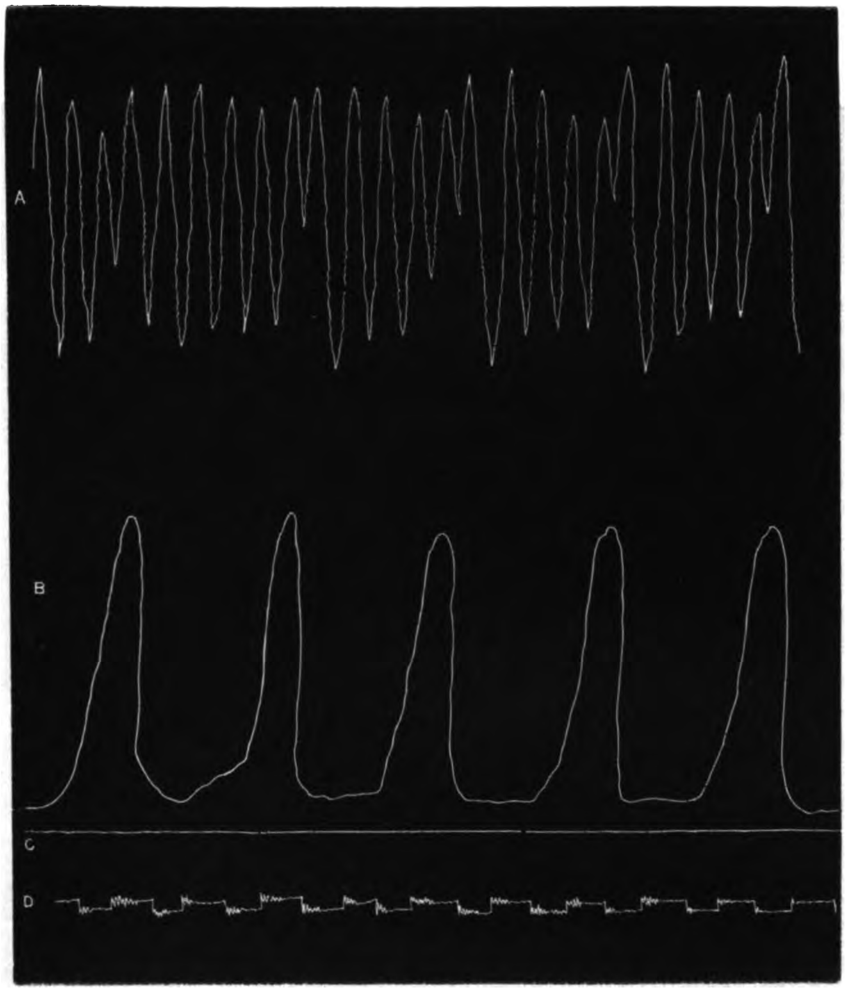
We will now consider the changes secondarily produced on the heart beat, *i.e.*, a few seconds after the shot had taken effect, until the end of the experiment.

Secondary Effects.

(*a.*) *Rhythm.*—In the cases where artificial respiration was not resorted to, and where consequently the animal speedily succumbed, the rate of the heart remained perfectly unaltered.

It was, however, quite otherwise when artificial respiration preserved the vitality of the nerve centres so as to lead to restoration of normal respiration, the exercise of which latter function permitted such effects to develop as of necessity follow the accumulation of blood extravasated within the skull. Should the bullet divide several vessels and cause a considerable effusion of blood in its track, then, in spite of the fact that some of the fluid and pulped brain substance escapes from the aperture of entry, the intra-cranial tension commences to rise as soon as the bullet is within the cavity, as is shown by direct measurement, see p. 239, and then there begins a slowing of the heart rhythm. A good example of this is evidenced by Experiment No. 48, of which we append the following details, and by Experiment 9, see fig. 2.

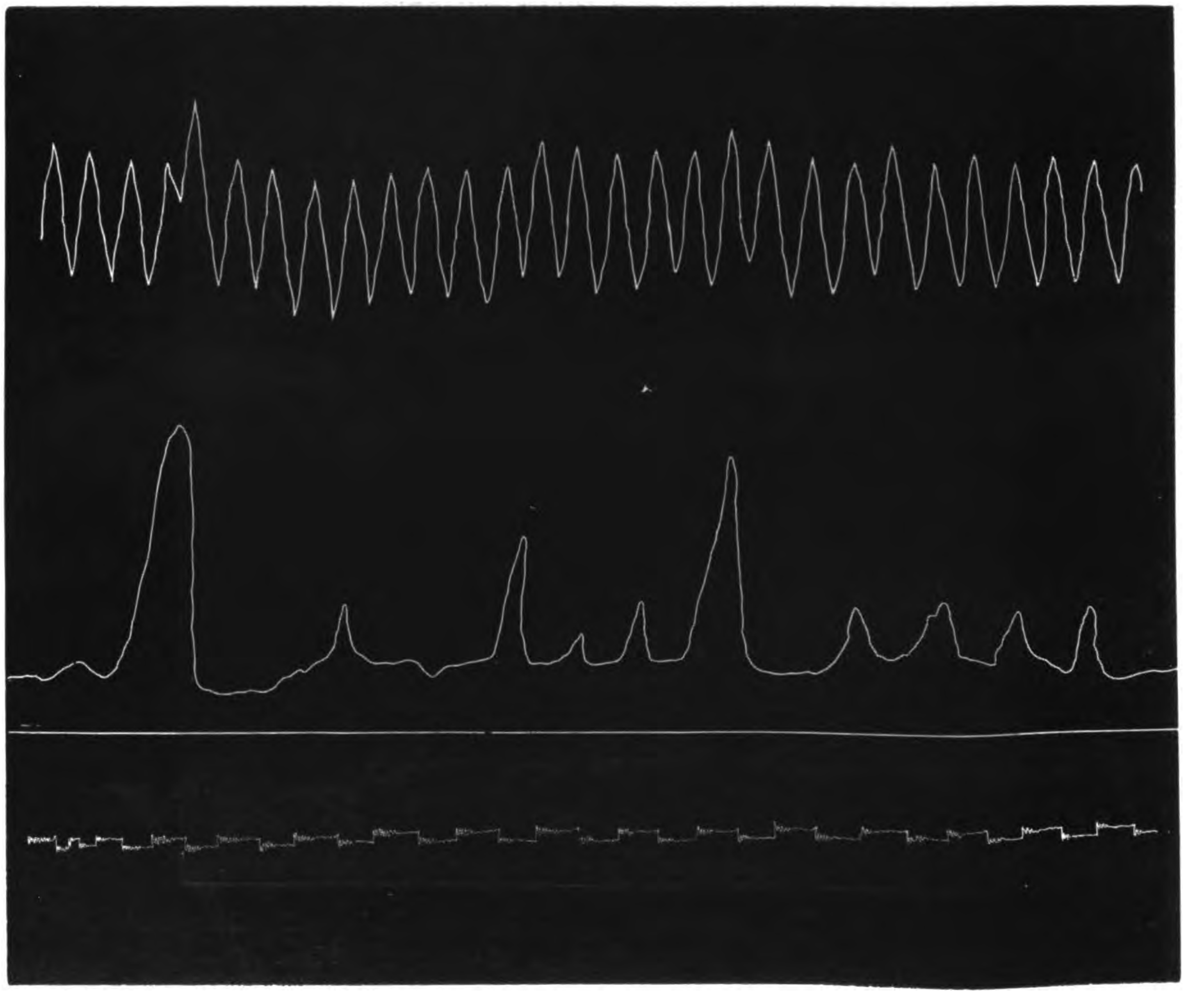
Fig. 2.



Tracing showing vagus effect. The respirations had recovered after artificial respiration.
A = central femoral blood pressure. B = respirations. C = shot signal line. D = seconds trace.

	Rhythm.
Before the shot.	11 beats in 4 secs.
Shot.	——
10 seconds after shot.	7 beats in 4 secs.
1 minute after shot.	5·5 " " "
3 minutes after shot.	4·5 " " "
3 minutes after shot.	Both vagi divided.
7 minutes after shot.	11 beats in 4 secs.

Fig. 3.



Terminal phase of vagus effect, showing very slow heart rhythm and marked irregularity of respiration. Dog 9.

From this instance it is seen that the heart beats progressively slower in rate (for alteration in character *vide infra*), but that the original rhythm is restored as soon as the vagi are cut.

The phenomenon, therefore, is an example of the well-known effect (Leyden) produced through excitation of the vagus centre by raising the intra-cranial tension.

(*b.*) *Force.*—As regards the force of the heart beat, the amplitude of the excursions of the manometer column shows, on the whole, a steady increase parallel with the slowing of the rate until a well-marked "vagal" type of beat is produced. This parallelism is preserved so long as the blood-pressure is maintained. Should this latter fall, it is then noteworthy that the cardiac beats are also lessened in height, suggesting that the former phenomenon is due to the latter.

The amplitude of the "vagal" beats is sometimes enormous. We have measured such beats and found the mercury to execute excursions of 40 millims. in height with each ventricular systole. Section of both vagi causes, of course, the vagal character to entirely disappear. See the table on p. 230. We have often observed this vagal effect to develop in the complete absence of any primary change, thus establishing the truth of the view that it is evoked, not by the bullet, but by the secondary supervention of hemorrhage. When there is no vagal influence of the kind above described, and the heart gradually comes to a standstill, then the force of the ventricle steadily diminishes to the end of the experiment (see fig. 3).

C. *Vaso-motor Phenomena.*

Under this heading we propose to discuss the marked alterations we have observed to occur in the blood-pressure, and, in analysing the same, to indicate how far such variations may be attributed to the action of the heart or of the vaso-motor centre respectively. In nearly every case the pressure of the cardio-arterial trunk division of the vascular system was recorded by a cannula placed in the central end of the femoral artery, and in a few instances that of the common carotid.

To differentiate as far as possible the central vasomotor influence from that of the heart muscle, a cannula was in very many experiments also placed in the peripheral end of the opposite femoral artery; and in a few cases, as will be described later, a cannula was placed in the peripheral end of one carotid artery.

The phenomena observed appeared to us to be divisible into three stages, as follows:—

Stage 1. Fall of pressure at incidence of shot.

Stage 2. Recovery of pressure, and over-restoration of the same: "asphyxial rise," *vide infra.*

Stage 3. Variations in pressure between the occurrence of restoration of pressure and the end of the experiment.

Stage 1.—*Fall of Pressure at Incidence of Shot.*

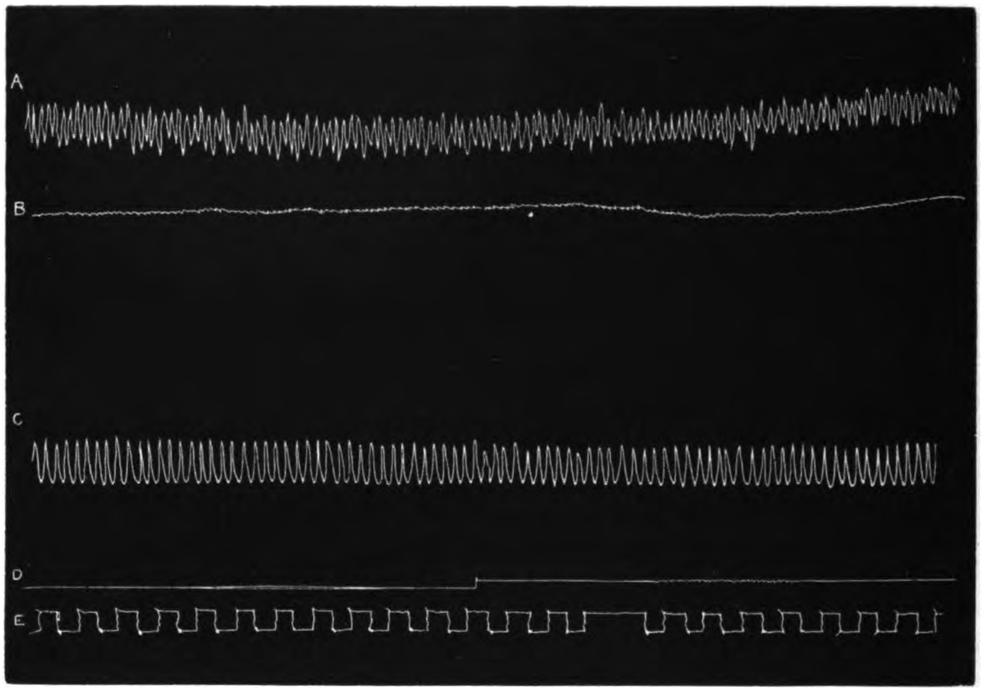
The moment of penetration of the skull is attended by a distinct fall in the blood pressure (see fig. 7 *et seq.*). The amount of this fall, however, is most inconstant;

we therefore placed together, in diagram form, tracings of the upper border, *i.e.*, uniting the systolic apices of the curves obtained by us in successive experiments, and analysed the combination of these curves.

The character of the fall is as follows :—There is a sudden interruption of the level of pressure, which then descends relatively rapidly (*i.e.*, in 10 to 15 seconds) to a minimal point, from which it as soon rises again.

The cause and mechanism of the fall are difficult to discover. In the first place, it is not dependent, as the respiratory arrest is, upon the penetration of the skull, for we have sometimes observed it in cases where the bullet did not penetrate, but merely glanced from the convex surface of the skull, or where it caused but a slight depression of the same. As a general rule, a glancing shot caused no change (see fig. 4).

Fig. 4.



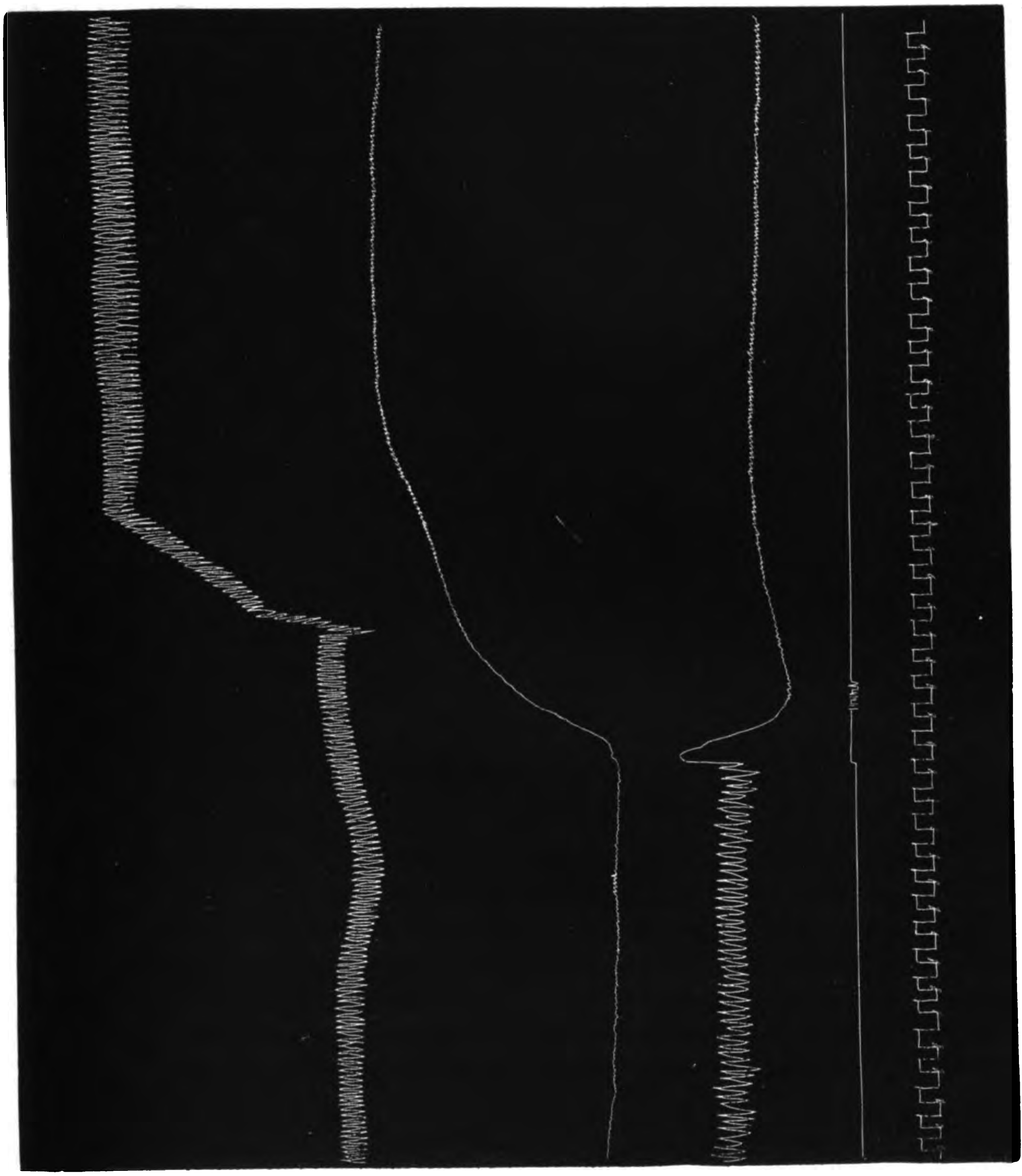
Tracing showing that there is little effect on the respiratory and circulatory system if the bullet glance from the surface of the skull without penetrating.

A = central femoral blood pressure. B = peripheral femoral pressure. C = respirations.
D = shot signal trace. E = seconds trace.

Further, when we removed the cranial vault (see page 242 and Experiment 67) to abolish, in great measure, the reflexion of the lateral pressures during the passage of the bullet, the fall was nevertheless well marked, and as fully developed as in cases where the skull was intact.

Finally, we obtained the same fall, even after both vagi and splanchnic nerves had been previously divided.

Fig. 5.



Tracing to show the correlation of the peripheral and central blood pressures with an unusually rapid rise of pressure (so-called asphyxial rise). Dog 49.

From consideration of the foregoing, we are compelled to believe that the initial fall is not due to a primary excitation of the vagal centre stimulated by the sudden increase of the intra-cranial tension. Under these circumstances, this depressor phenomenon appears to us to be a reflex effect on the heart, due to excitation of sensory nerves in the skin, muscles, bones, and dura, mechanically irritated by the bullet; because, whatever the arrangement of the experiment as above detailed, the penetration of one or more of these tissues was a constant feature.

Where the fall of blood pressure is most marked, the heart beats, as registered by the manometer (central, *i.e.*, cardiac, cannula), are much smaller in amplitude. This is what was to have been expected if the fall of pressure is brought about as explained above.

The final analysis of Stage 1, with the aid of the peripheral manometric observations (see below), will be found to completely confirm the foregoing conclusions.

Stage 2.—Recovery of Pressure and Over-restoration of same ("*Asphyxial Rise*").

In almost every case the blood pressure recovered itself after the preliminary fall just described, and regained its former level. Further, in all cases in which the respiration was arrested, and an asphyxial state thereby developed, the restoration of the blood pressure was continued as an asphyxial rise (see fig. 5 for a very marked effect). In those cases in which the respiration was not arrested, but in which nevertheless there was an initial fall, there was no over-compensation. So, too, where an apnœic condition existed the rise was less or not present (see fig. 6, p. 236). Wherever, on the other hand, respiration ceased, the over-compensation became very marked. The peripheral blood-pressure rose in exact parallelism with this "asphyxial rise" of Stage 2 (see also *infra*).

Stage 3.—*Variations in Pressure between the Restoration of the same and the End of the Experiment.*

After the blood-pressure had returned to its former level in cases where the asphyxial arrest of the respiration did not occur, it tended to fall gradually, and this slow fall was marked by the occurrence of sundry small variations in height, producing curves of a TRAUBE-HERING character.

The same curves may also be seen developed in imperfect parallelism on the record obtained from the peripheral end of the femoral artery, and are therefore doubtless truly of central vaso-motor origin (see Experiment 49).

Results obtained by the use of the Peripheral Manometer.

We have employed peripheral manometric observations in two ways, by fixing the cannula, firstly, in the peripheral end of the femoral artery, and, secondly, in the peripheral end of the common carotid artery. As the distribution of the latter is intracranial, we place the results obtained therefrom in a separate paragraph.

(A.) *Peripheral Femoral Observations.*

The results obtained from the femoral artery prove distinctly the following conclusions:—

(1.) That the pressure in the peripheral arterioles after the shot, follows in a strikingly parallel manner the variations of pressure in the cardiac arterial trunks, though later and in a more gradual manner (see fig. 7).

(2.) That the initial fall described as occurring in Stage 1, *i.e.*, immediately upon the bullet perforating the skull, is, in the majority of cases, similarly exhibited in a (later) parallel fall of pressure in the peripheral femoral arterioles. In two instances out of fifteen experiments made on this point, however, there was no fall recorded on the peripheral trace. It is therefore clear that the initial fall in the central blood pressure, is certainly not a vaso-motor phenomenon, a conclusion already arrived at on page 234 from other considerations, and to which latter may be now added the fact that the effect is produced within the brief period of time required for a single reflex act, and not a period sufficient for an excitation of the vaso-motor centre to evidence itself by its usual curve of reaction.

(3.) That the ratio between the central, *i.e.*, cardiac blood-pressure and the pressure observed in the femoral arterioles is little altered by the effect of the shot, and the figures obtained show only the fact that the cardiac or arterial trunk pressure is lowered before the peripheral.

The average ratios obtained are as follows:—

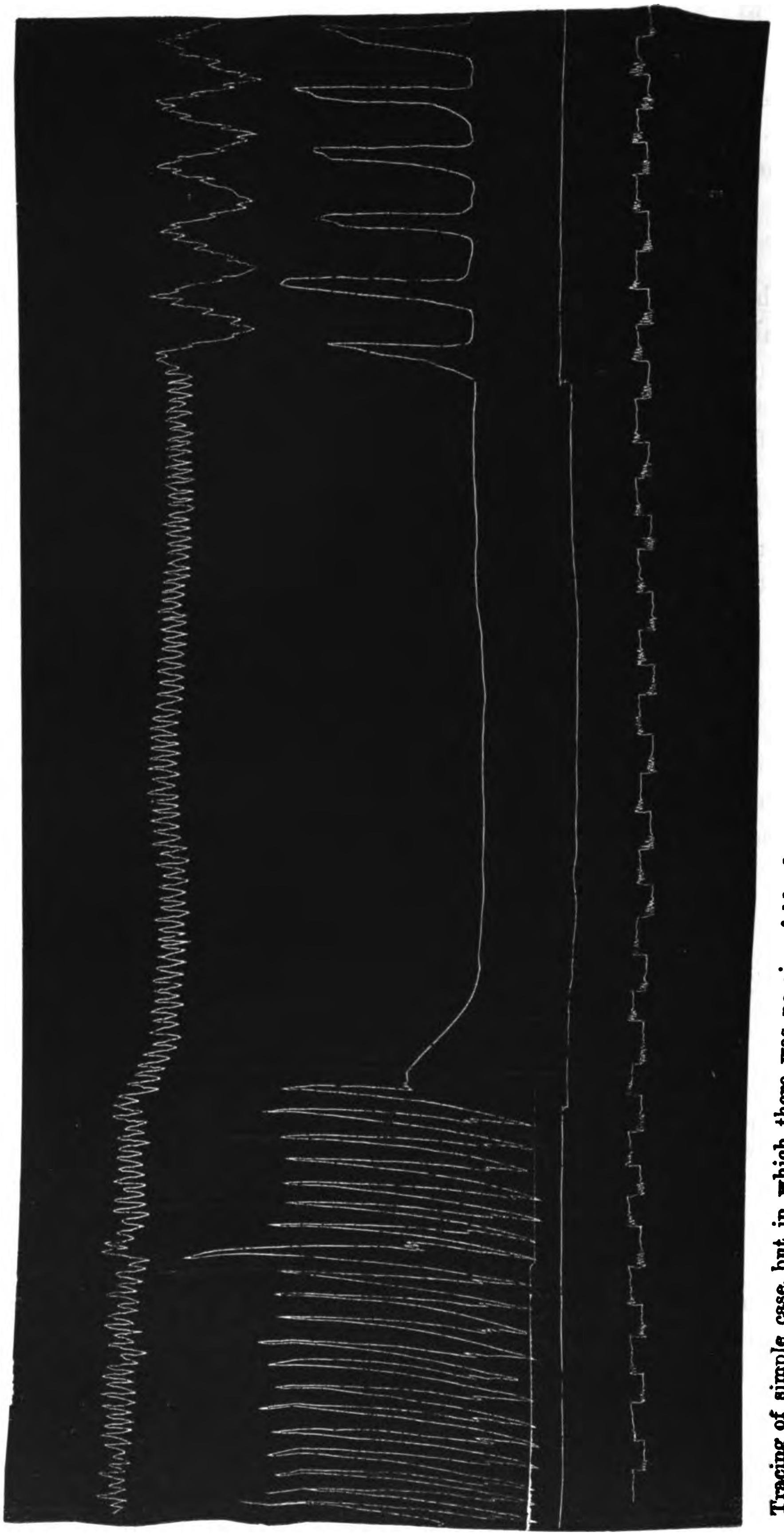
	A. Before the shot.	B. 2 mins. after shot.	C. Later but variable periods, 6–20 mins. after shot.
$\frac{\text{Cardiac pressure.}}{\text{Peripheral pressure.}}$	$\frac{2 \cdot 8}{1}$	$\frac{2 \cdot 25}{1}$	$\frac{2 \cdot 2}{1}$

The general effect indicated by these ratios is that already described from examination of the tracings. From these facts we are led to believe that the vaso-motor nerve apparatus is, if at all, very slightly primarily affected by a bullet wounding the cerebral hemisphere.

(B.) *Peripheral Carotid Observations.*

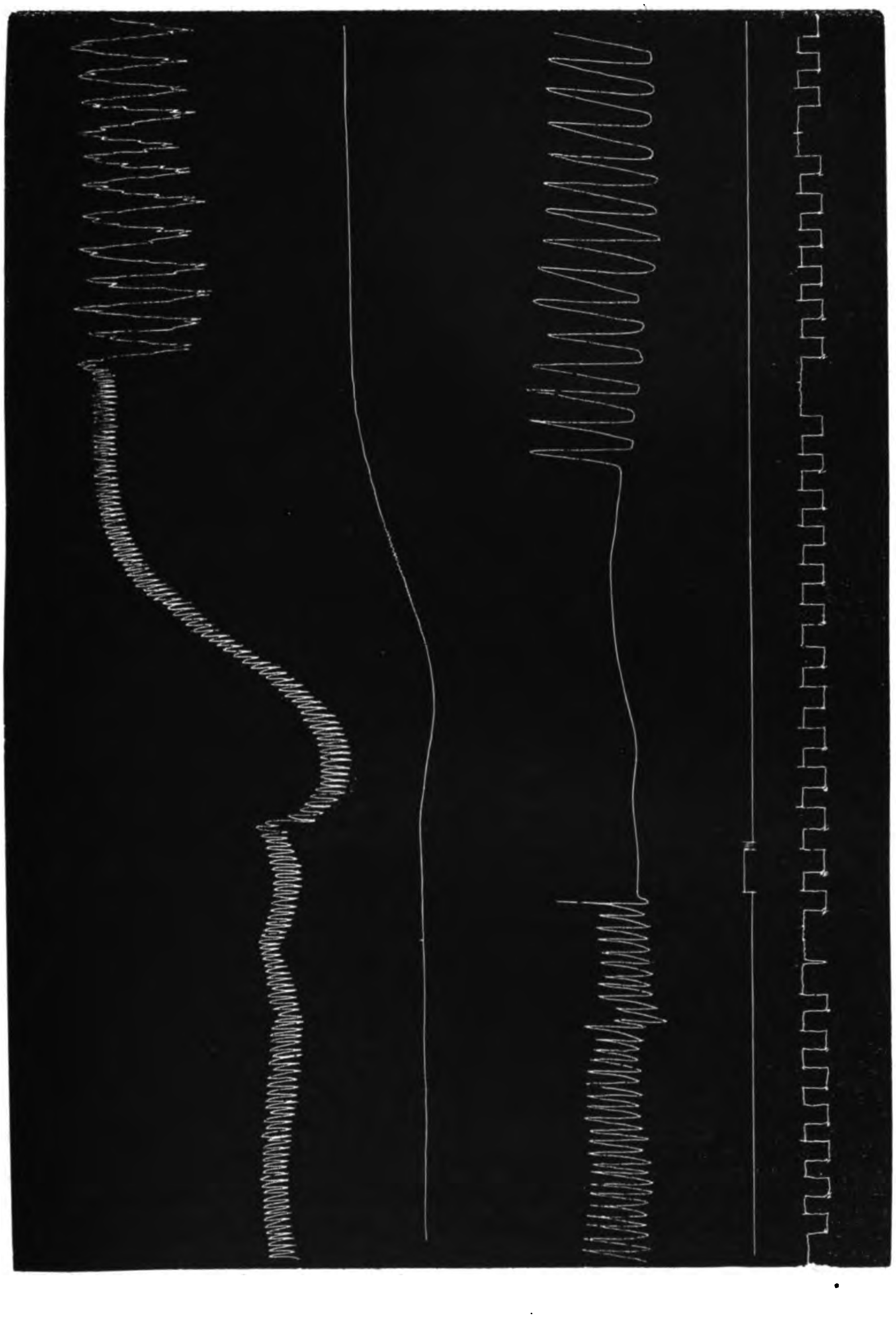
In considering the changes produced in the pressure within the distribution area of

Fig. 6.



Tracing of simple case, but in which there was no rise of blood pressure of asphyxial kind. Note great depth of respiratory movements before shot. Dog 9.

Fig. 7.



Tracing to show the character of the rise of blood pressure in the peripheral end of the femoral artery; and the correlation with the central femoral pressure curve. Dog 40.

the carotid two preliminary facts have first to be remembered, viz.: (*a.*) That the bullet cuts open numerous branches of the artery. (*b.*) That the intra-cranial hemorrhage gradually brings about compression of the artery and its branches. It is clear at the same time that these two facts tend to neutralise one another in time, *i.e.*, as the blood continues to be extravasated. Further, not only at the incidence of the shot, but also later, it is not unlikely that the cannula in the peripheral end of the carotid may act in part as that of an intra-cranial manometer.

The results actually obtained are as follows:—

The fall of pressure in the peripheral carotid cannula is very sharp (see fig. 8, p. 240), and markedly contrasts with the slow and imperfect fall in the peripheral end of the femoral artery. See Experiments 42, 52.

After the shot the pressure rises and subsequently exhibits a tendency to parallelism, but not so markedly as in the case of the femoral.

On examining the ratio between the central and peripheral pressures, we find the following averages:—

	Before shot.	After shot, 2–6 mins.
Cardiac pressure. Peripheral carotid pressure.	$\frac{1\cdot76}{1}$	$\frac{2\cdot53}{1}$

This establishes the fact, above described as being elicited from inspection of the tracings, that the fall in the peripheral pressure is greater than that of the central, whereas, in the case of the peripheral femoral, this was not the case. The general character of the carotid fall, especially the suddenness, suggests strongly to us that it is in part due to the simple effect of the bullet opening the skull, and also to the wounding of the branches of the carotid.

D. *Muscular System.*

With the object of finding whether the mechanical effect of the passing bullet also caused in reality an excitation of such fibres, etc., as are sensitive to mechanical stimuli, we investigated the condition of the muscles. To ordinary attentive observation, the muscles of the limbs and trunk are easily seen to twitch at the moment of shot. For the purpose of recording such phenomena we attached the freed patellar tendon of the rectus femoris muscle to a Fick spring myograph. Fig. 9 is a good example of what occurs.

As the bullet traverses the hemisphere the rectus sharply contracts and the contraction then gradually relaxes. That this is a genuine excitation effect exerted upon the encephalon (possibly on the fibres of the corona radiata) we proved in several experiments by dividing the spinal cord in the mid-dorsal region before shooting, in which case the muscular phenomenon was absent from the muscles supplied below the level of the section.

From the foregoing description it is evident that a very marked and remarkably constant series of phenomena are evoked by the passage of the projectile. It now remains for us to point out how the various events are produced, and to show that in all probability they occur in consequence of the medulla oblongata being subjected to the shock of considerable pressure suddenly applied.

PHYSICAL CONSIDERATIONS UPON THE CAUSATION AND MODE OF PRODUCTION OF THE ABOVE DESCRIBED PHENOMENA.

For the purpose of this paper the skull may be considered as a rigid capsule filled with soft solid and fluid contents. The projectile may be considered as a cone driven with great velocity. The "active" force exerted by a cone at any given point, driven into a rigid mass, varies directly as its momentum and the angle of the inclination of its surface. By far the largest factor is, of course, the momentum, and variations of this would practically produce all the variations of the effective force exerted by the bullet during its passage through the brain. We may consider that lines of force operate from every point on the surface of the bullet in directions perpendicular to the particular part of the surface considered. Owing to the soft solid and fluid state of the contents of the skull, such forces would be transmitted without much diminution to the surface of the brain. On arriving at the unyielding skull they would be reflected back from every point of its inner surface, so that the active force of the bullet would immediately become a "compressing" force operating on the general intracranial contents. This conclusion, drawn from general theoretical physical considerations, is borne out by the phenomena related above, since the effects we have described are really those of severe acute cerebral compression, as stated by SPENCER and HORSLEY* to follow noteworthy elevation of intracranial tension. To record the chronology of these events, and especially the rise of tension more accurately, we employed the method described on page 225 for marking the moment and nature of changes in the intracranial tension. The graphic records obtained by this method are well instanced by fig. 10, p. 244, in which it is seen that there is a very sudden increase of the intracranial tensions at the incidence of the bullet, and that the tension continues to increase after the initial rise until an equilibrium is arrived at, this increase being clearly due to the secondary supervention of hemorrhage within the skull. The extent of the damage, and the inevitably fatal effect (by the respiratory centre being unable to recover its function) of the larger bullet we used in our experiments is now fully explained. These positive considerations have been fully confirmed by negative experiments, in which it has occasionally happened, when employing the pistol, that through faulty cartridges, &c., the velocity of the bullet was so reduced that it was only just able to penetrate the skull. In such cases, the phenomena were proportionately less developed, so much so indeed that in one instance (1 out of 75 experiments) the respiration, though extremely depressed, was not absolutely arrested, notwithstanding the fact that the track of the bullet occupied the same region as in other cases in which the force was greater. The last series of our experiments were directed towards this very point, and are, we think, conclusive in demonstration of the truth of the explanation we have given above. The design for these experiments was as follows:—

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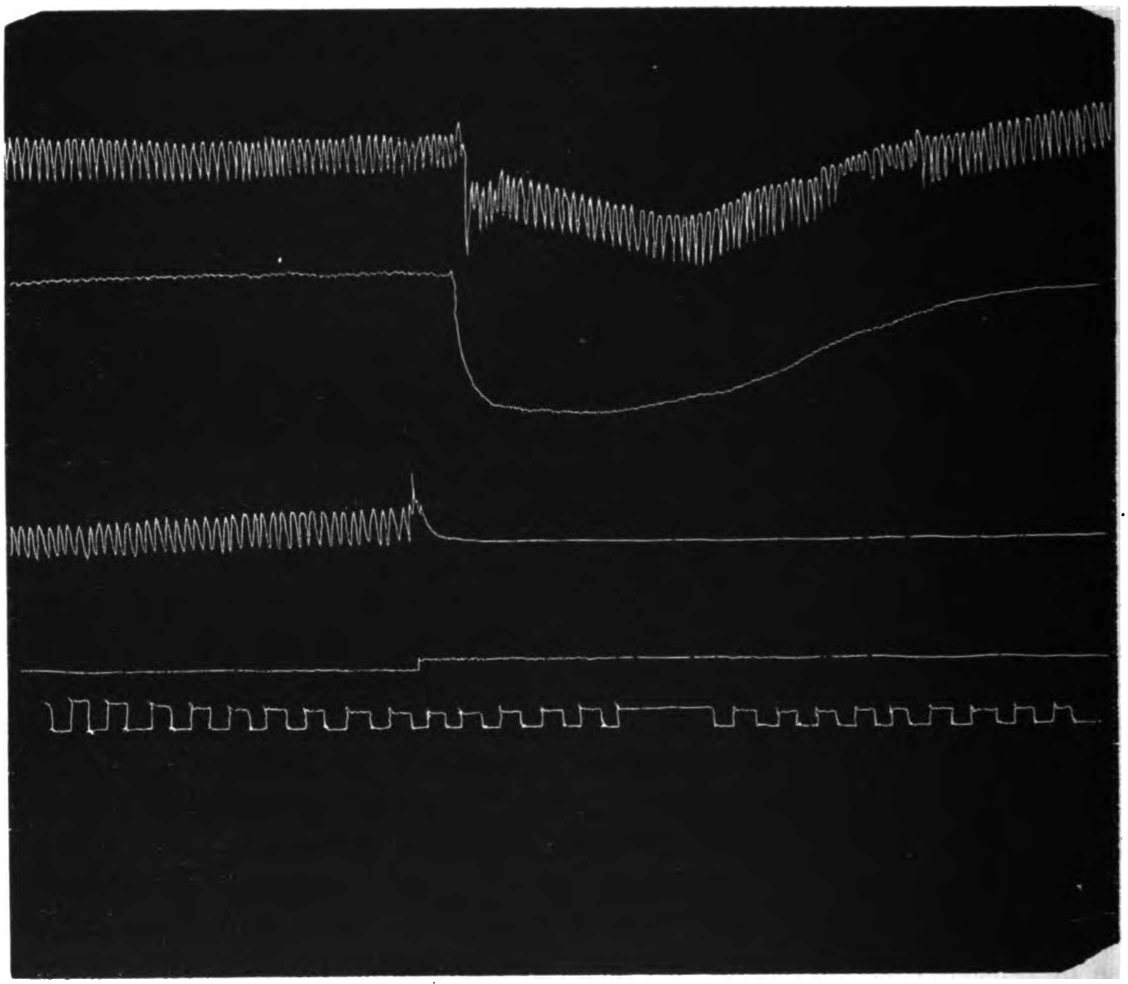
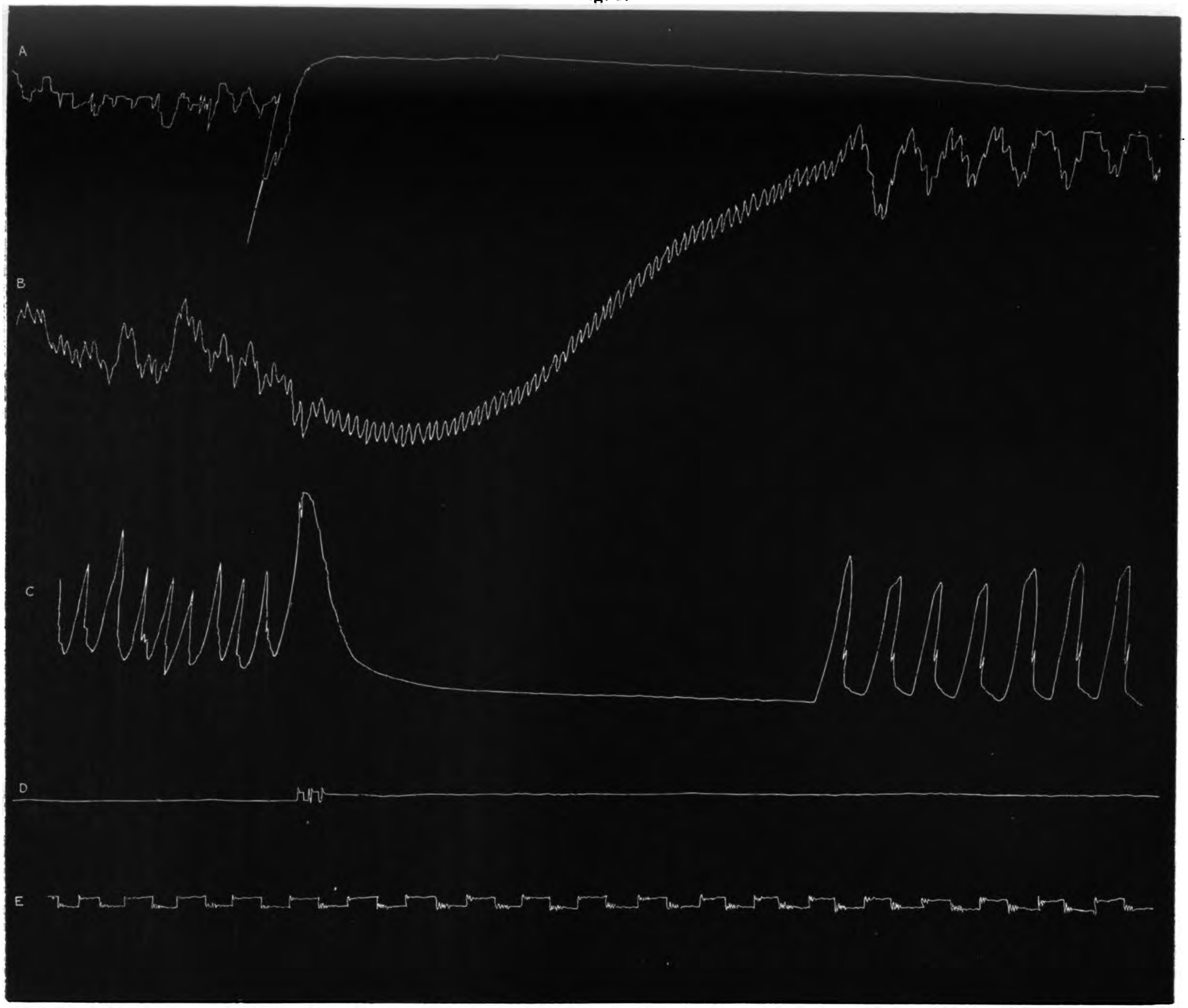
* 'Phil. Trans.,' B, 1891.

Fig. 8.



Cannula in the peripheral end of the left carotid artery. Note the suddenness of the fall of pressure. Dog 42.

Fig. 9.



Tracing showing the sudden contraction of the rectus femoris muscle at the moment of shot. Note the tremor in the muscle due to etherisation (ether clonus so-called) before the shot.

A = tracing from myograph lever. B = central femoral pressure. C = respiratory trace. D = shot signal trace. E = seconds trace.

Supposing the above stated physical considerations to be true, it seemed to us that if part of the rigid wall of the skull were removed and the dura mater opened, that the lines of force could not be reflected, and that, consequently, the forces which exerted the unfavourable effect upon the respiratory centre when the skull was intact, would be dissipated in projecting the brain peripherally, *i.e.*, through the opening. In an experiment of this kind a certain portion of the occipital lobe is seen to be forced at the moment of shot through an opening in the parietal bone. (See fig. 3, of Plate 3.) This expulsion of the cranial contents would be contributed to, of course, by reflection from such points of the cranial surface as remained. In a certain number of experiments, therefore, to test these conclusions, the skull and dura mater were very freely taken away, the entire parietal and occipital lobes being exposed, and the animal was then shot through the frontal bone and region of the brain.

Under these circumstances almost the entire hemisphere was torn off by the bullet and scattered on objects around. Although such very extensive injury was inflicted on the cerebrum, no respiratory arrest occurred (see fig. 11), for the reason suggested, that in consequence of the rigid capsule of the skull being in great measure removed, the medulla oblongata was no longer subjected to the severe compressing forces above discussed.

We now pass to the further consideration of the physical conditions which underlie the development of the disruptive lateral forces just referred to. The idea that some of the so-called explosive effects produced by bullets passing through soft and moist structures, were due to hydrodynamic forces, arose apparently with HUGUIER, who made a number of experiments relating to the effect of bullets upon hard and soft structures, and in which he speaks distinctly of the lateral pressure of a projectile striking a moist object as throwing to a distance fragments with the contained liquid; and further, in describing the effects upon parenchymatous organs, *e.g.*, the brain, he says: "Il semblerait que le liquide abondant que renferment tous ces organes parenchymateux, projeté au loin par l'action latérale de la balle, aît entrainé avec lui des portions de ces viscères."*

But perhaps the most light has been shed on this subject by the researches of Professor KOCHER.

In the first place as regards direct hydrodynamic effect upon the skull, KOCHER found that if the foramina in a dried skull were plugged with plaster of Paris, and the cranial cavity then filled with water, that the passage of a bullet (Vetterli rifle) through the preparation, burst the skull into pieces, the rending beginning in some places in the sutures. To investigate the influence of water interstitially present in substances, he fired numerous bullets through tin-plate canisters, open and closed, filled with dry and wet substances respectively. Whereas the dry filled canisters were merely perforated by the projectile, those filled with wet substances were burst explosively when penetrated by the bullet.

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* 'Bulletin de l'Académie Nationale de Médecine,' tome 14, 1848–49.

KOCHER also[*] showed that a projectile with less propulsive force produced much less bursting effect.

The conclusion he arrived at was that the "explosive" effects of bullets through the brain were due to the lateral pressures in wet substances being hydrodynamic in character.

REGER[†] from his earliest experiments in 1882 confirmed the hydrodynamic view so firmly grounded by KOCHER.

In his second paper he shows very definitely the extent of the error that has been made in many observations on tissues that are dead, and consequently more rigid. We have ourselves in this respect established a striking contrast as regards the effect of the bullet on the brain, by first firing a bullet through it in the living condition, then hardening the brain in MÜLLER's fluid, and again shooting it in another region. In the former case the bullet tears a large funnel-shaped passage, with much bruising. In the second case it simply bores a hole with one or two lateral diverging cracks.

BRUNS,[‡] in a paper descriptive of the surgical aspect of gunshot wounds, describes a large series of experiments made by him on the effect of the small calibre rifle bullet on tissues, &c. From a direct manometric observation of the pressure set up by the bullet's passage, he describes a rise of pressure equivalent to that of fifteen atmospheres.

In all cases the most "explosive" effect was observed in the case of the brain in the skull, the control being evidenced by the simple perforations of skulls emptied of their contents.

A general survey of the results obtained by BRUNS shows that the bursting effect is in proportion to the velocity of the projectile; and we have repeated KOCHER's experiments, and have in every respect completely confirmed them. In view of the fact that, so far as we are aware, no illustrations of such experiments have been published, we append photographs of some of our own results.

Plate 3, fig. 4, shows photographs of two dried dogs' skulls of similar strength. The skull shown as intact was fired at with a saloon pistol 22 cal., and merely perforated, as is shown in the photograph. The other skull, which had been cleaned in precisely the same way, was fired at with the same pistol after the cranial cavity had been filled with water and all the foramina closed with modeller's wax. The rending effect of the water, starting the sutures, &c., is particularly well shown. It may be

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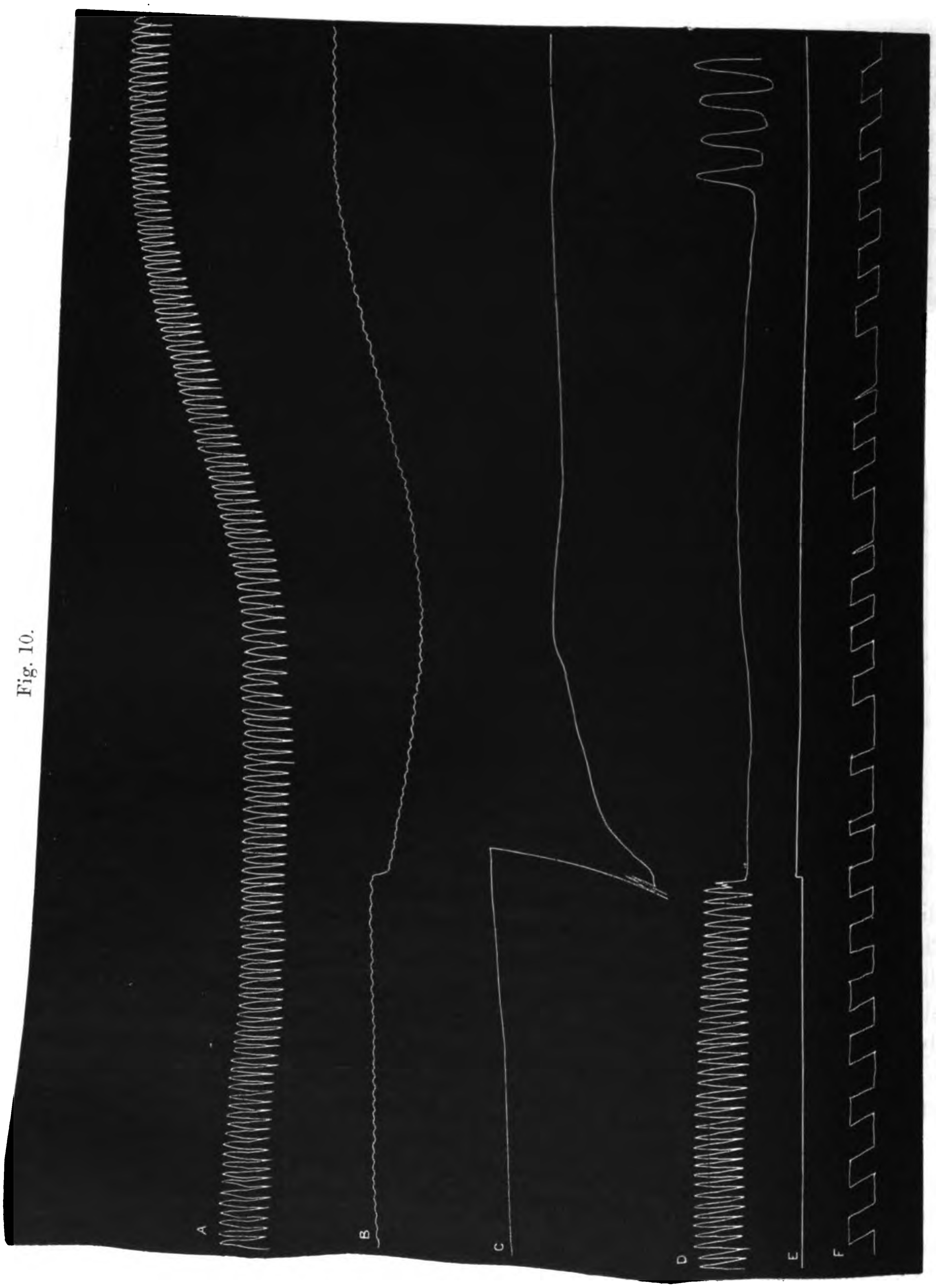
[*] 'Correspondenz-Blatt für Schweizer Aerzte,' 1875, p. 3; 1879, p. 65.

[†] 'Gewehrschusswunden der Neuzeit,' 1884; 'Verhandlungen der Deutschen Gesellschaft für Chirurgie,' Berlin, 1892.

[‡] 'Verhandlungen der Deutschen Gesellschaft für Chirurgie,' 1892, p. 1.

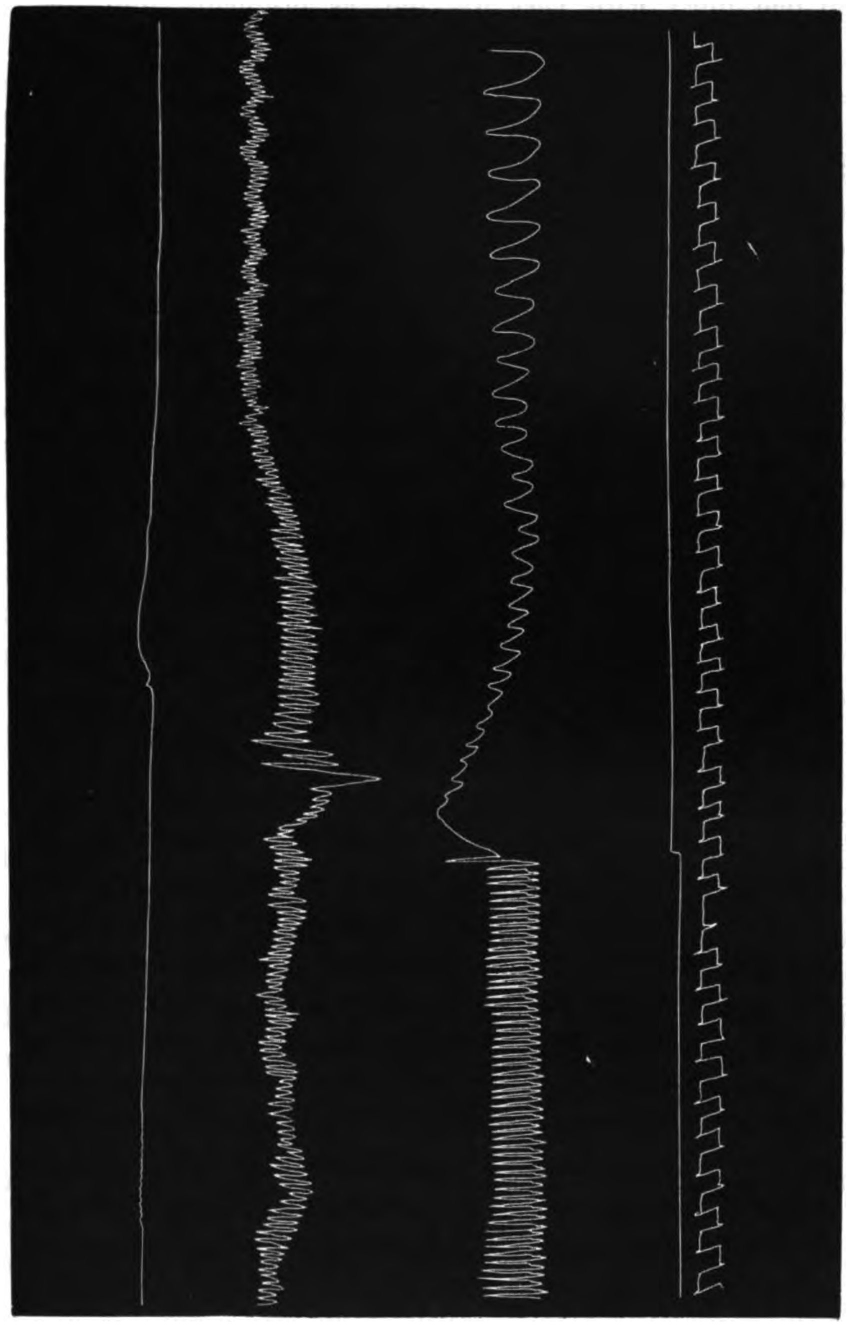
Fig. 10.



Tracing showing the rise of intracranial tension at moment of shot. Dog 60.

A. Central femoral blood pressure. B. Peripheral femoral blood pressure. C. Intracranial tension. D. Respirations. E. Shot signal. F. Seconds.

Fig. 11.



Cranium opened freely before the shot. Respiration not arrested, though inspiratory spasm produced, and diminution of movements.

noted, too, that the effect is greatest on the side of entry of the bullet (*vide* p. 248). Precisely the same influence is seen in a very marked degree when the ·38 cal. bullet passes through a similar skull containing the brain in the living state. Finally, we have observed the same difference between the effect of the bullet on a canister full of dry lint and one filled with very wet lint, as originally described by Professor KOCHER.

A ·38 cal. bullet was first fired through the dry canister, and merely perforated it, whereas when a similar bullet was fired into the wet one, it completely blew it up, projecting the contained lint even on the top of a tall wooden block placed behind the canister to prevent the bullet injuring the wall.

On the further question, what is the quantitative character of the hydrodynamic effect produced on water at different points after entering the fluid, it occurred to us that the bullet might be made to automatically record the disturbance it produces, and as follows. A tinplate box 12 in. by 10 in. by 8 in. was taken and filled with water coloured strongly with methylene blue. A white unglazed paper screen was then fixed longitudinally, the bottom part touching the surface. The bullet was then placed so that it travelled through the water just in front of and parallel to the bottom of the screen, and at a depth of 2 centims. The effect was that a wave of water was thrown up by the bullet and against the white screen, which was consequently stained blue by the wave. A number of such experiments produced a good series of such records. In these it is seen that the disturbance of the water is greater almost immediately after the bullet enters the water, and then falls gradually to the end of the bullet's trajectory.

In the course of these experiments we found that the disturbing effect of the bullet was, as may be supposed, greatest in the immediate neighbourhood of the trajectory, but we were not prepared to find that when the bullet was fired through a weak, *i.e.*, a wooden box, close to (2 centims. distance) one side, that that side was alone burst out. It is interesting to observe that the water surface in all these experiments was only subject to the atmospheric pressure. So, too, on *post mortem* examination of the skulls experimented upon, in those cases where the bullet did not penetrate the further side of the cranium, the proximal side was the more severely rent. (*Cf.* also fig. 4, Plate 3.)

It may, perhaps, be useful to refer here to the theory first formulated by HAGENBACH,* contested by BODYNSKI,† and re-asserted by HAGENBACH,‡ namely, that a bullet coming into contact with a rigid body loses a certain proportion (27 grams. from a bullet weighing 40 grams., moving while 100 paces from the firing point with a velocity of 320 metres per second) of its substance by melting, and so produces additional destruction. This notion of fusion of the bullet received much clinical support from SOCIN,* who made, in conjunction with HAGENBACH, experiments of deformation and loss of substance of projectiles striking hard substances. In no case, however, was it proved that the condition of the bullets was due to melting. Although much discussed by them, curiously enough none of these authors seem to have adopted the course of testing the matter by actual experiment.

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* POGGENDORFF'S 'Annalen der Physik und Chemie,' vol. 140, 1870, p. 486.

† POGGENDORFF'S 'Annalen der Physik und Chemie,' vol. 141, p. 594.

‡ POGGENDORFF'S 'Annalen der Physik und Chemie,' vol. 143, p. 153.

The matter remained in this unsatisfactory state until VON BECK† adopted a rough calorimetric experiment, from which it was obvious that HAGENBACH'S theoretical position was unsound.

A very conclusive research negativing the heating of the bullet at least by friction in its course is that of MESSNER.‡ He fired small-bore bullets through canisters filled with sterilised meat peptone gelatine, the bullets in some cases being clean (control experiments), in others infected with cultures (micrococcus prodigiosus, green pus, staphylococcus pyogenes being used) and also (when clean) caused to pass through a layer of flannel on which a culture had been spread before entering the canister. The results invariably showed that the bullet carried in the organisms, and that the latter were in nowise destroyed by the heat supposed to be developed.

By many authors, *e.g.*, BUSCH,§ the fact that fluid fat sometimes oozed from the wound was taken to mean that it was melted by the heat of the bullet. This is put forward without recognition that fluid fat always escapes from adipose tissue if this latter be cut, lacerated, or contused. Against the view that any part of the bullet is fused, is the incontrovertible and finally decisive fact, that fired bullets often show the marks of the rifling of the barrel, and scratches on their surfaces as perfectly sharp. In one case we noted, as VON BECK had previously, that the bullet had enclosed a hair in its course, which hair was quite uninjured. Finally, no part of the wound is in the slightest degree charred, even superficially.

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* 'Chirurgische und Pathologisch-Anatomische Beiträge zur Kriegsheilkunde.' Leipzig, 1872, p. 10.

† *Loc. cit.*

‡ MESSNER. "Wird das Geschoss durch die im Gehirnlauf stattfindende Erhitzung sterilisirt?' 'Münchener Medicinisches Wochenschrift.' No. 23. 1892.

§ 'Archiv für Klinische Chirurgie,' Bd. 16, 1874, p. 22.

DESTRUCTIVE EFFECT OF THE BULLET ON THE ENCEPHALON.

The destruction caused by the bullet may be described under two divisions, viz., (1) immediate effects, (2) remote effects.

1. *Immediate Effects.*

The local destruction caused by the bullet in the brain is well shown in all our specimens. As **HOPPNER** and **GARFINKEL**[*] have demonstrated, the track of the missile is a funnel-shaped tube, the wide end of the funnel corresponding with the aperture of entry. We find that in the case of the pistol bullet the aperture of entry is a round, depressed, and lacerated opening, with blood extravased into the pia mater around for a distance varying from 5 to 15 millims. The canal of the bullet is a rounded tube with ecchymosed pulpified walls, the softening extending through the substance of the hemisphere for about 1 centim. on each side. The aperture of exit is a ragged and bruised opening. The bullet named (No. 3) frequently did not penetrate the encephalon completely. Under these circumstances the bullet was found resting at the end of a canal which exhibited progressively less and less bruising. Such diminution of the bruising effect is well described by **KLEBS**, who showed that with the cessation of the movement of the bullet the track of the bullet was simply represented by a canal showing loss of substance.

In every case the canal contained fragments of bone which were often found on the proximal side of the aperture of exit, having been driven through the encephalon, and in several cases a disc formed from the squamous bone, and rather larger than the bullet, was forced half-way into the hemisphere opposite to the side fired at.

The laceration of the canal must thus in part be attributed to the movement of these fragments of bone, but the pulpy state of the walls can only be due to the lateral thrusting forces of the bullet referred to on page 242, &c., and which were described by **MURON**[†] as producing like effects at a distance in other soft tissues, *e.g.*, muscle and marrow of bone. (*Cf.* **BUSCH.**[‡])

WAHL[§] also points out that the particles of the tissues at the point struck are thrust aside into the neighbouring structure, so destroying these. On this point **DELORME**[||] has urged that the lacerating effect seen so markedly when a bullet traverses a book is due to the bullet driving in front of it *débris* of the leaves struck first. That this is so will admit of no doubt in the mind of anyone who repeats the experiment. The punching action of the bullet leads to its driving in front of it particles of increasing diameter, and these by being hurried forward cause much destruction. Although in consequence of the difference in density analogy may easily be strained in transferring such results as these to explain the condition of the bullet tract through the brain, still relatively similar conditions must be present also in the latter case.

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[*] 'Centralblatt fur Chirurgie,' 14 and 15, 1874.

[†] 'Comptes Rendus des Séances et Mémoires de la Société de Biologie,' 1871.

[‡] 'Verbandlungen der Deutschen Gesellschaft für Chirurgie.'

[§] 'Archiv für Klinische Chirurgie,' vol. 17, Berlin, 1874, p. 56.

[||] 'Traité de Chirurgie Militaire.'

A further point which requires brief consideration is the suggestion of **BUSCH**[*] that the rotation of the projectile causes molecular disruption of the walls of the wound. So long as the bullet remains smooth the rotation of its surface cannot produce an appreciable effect even if such rotation were complete. But, further, the rotation exists during the intra-cranial passage of the bullet only to the extent of a fraction of the circumference of the latter. We may add that the rotation of the projectile is not regarded as a factor by practical artillerists in considering the disruption of penetration. So, too, **KOCHER**[†] shows that the only influence of the rotation would be to cause the particles to fly sideways from the front of the bullet.

In reference to the disruption of the walls of the bullet track allusion must be made here to the view frequently put forward, namely, that part of the effect is due to air carried forward by the projectile. The first allegation that the compressed air so beautifully shown in the photographs of the ·303 bullet *in transitu*, made by Mr. **BOYS**,[‡] is in great measure the source of the energetic action of the bullet on soft tissues was made by **MELSENS**.[§] Before him, the notion that projectiles cause lateral shocks and disruptive vibration by virtue of the wave of compressed air they produce, prevailed, of course, as a long-standing tradition. It was, nevertheless, already completely disposed of by the very accurate measurements made of the displacements, caused by such waves by **GROSSMAN** and **PELIKAN**,[||] who demonstrated that the air displaced laterally by a forty-pound cannon shot scarcely influenced a light registering apparatus, and had no effect on an animal even when the projectile passed quite close to its body. Moreover, from the point of view of pure physics, **MORIN**,[¶] in the discussion on **MELSENS**' paper, objected that the greater density of the object penetrated by the bullet would cause such reflection of the waves of compressed air as to preclude the possibility of their assisting to break up the object fired at. In Professor **BOYS**' photographs the reflection of such waves from the surface of hard substances, *e.g.*, glass plate, is well seen. In our experiments the conditions were very parallel, for before the bullet entered the brain it had to traverse the hard bony wall of the skull as well as tough aponeurotic membranes. As far as the direct entry (*i.e.*, no screen intervening) of bodies projected with a certain velocity into fluid is concerned, that is, of course, another matter. **Magnus**[*] having shown that a large quantity of air was entangled behind the projected body, and thus carried into the fluid, **Laroque**,[†] by a very ingenious experiment of a long falling body which would not entirely sink, found that some air was certainly driven into the fluid in front of the projectile. **Morin**'s objection, however, seems to us to completely nullify **Melsens**' conclusions so far as the conditions of our present research might be supposed to be affected by such air. **Wahl**[‡] believed that such air might enter a vein, and thus cause sudden death, but this belief, unsupported by any physical demonstration, must fall to the ground for the same reason as **Melsens**' hypothesis.

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[*] 'Archiv für Klinische Chirurgie,' vol. 16, 1874, p. 56.

[†] *Loc. cit.*

[‡] 'Nature,' March, 1893.

[§] 'Comptes Rendus de l'Académie des Sciences,' vol. 65, 1867, pp. 564.

[||] SCHMIDT's 'Jahrbücher,' 1859 and 1869. "Note sur les plaies produites par les armes à feu." 'Journal de la Société Royale des Sciences Médicales et Naturelles,' Bruxelles, 1872, p. 53.

[¶] See first reference to MELSENS, p. 568.

2. *Remote Effects.*

The remoter destructive effects of the bullet are extremely important, as to them are unquestionably due the secondary occurrence of general death, when the primary source, viz., the arrest of respiration, has been successfully met by the employment of artificial breathing.

The first and most important is the entry of blood into the lateral ventricles, and its passage thence by the aqueduct of Sylvius into the fourth ventricle. In cases where this occurred the respiratory centre could not be restored into activity. It is therefore well to consider the cause of this injection, as it were, of the ventricles with blood.

In the first place it is of course essential that the integrity of the ventricle should be interrupted by the bullet. It is, however, not sufficient for the production of this fatal result that the bullet should only open the ventricular cavity. The passage of the blood downwards is due to the pressure under which blood is extravasated into the intracranial cavity. Under ordinary circumstances, as we have shown, the intracranial tension rises very markedly at the moment of shot, and continues to rise as the secondary extravasation occurs. That this rise is the cause of the blood finding its way downwards is shown by the fact that in the experiments in which the cranial vault was removed, this passage of blood to the fourth ventricle did not occur, although the lateral ventricles were opened by the bullet. Besides, in many instances of excision of portions of the hemispheres, the ventricle is freely opened without harm, both in man and the lower animals. The influence of pressure, however, in these cases may produce the fatal injection just described, as one of us has witnessed.

Relief of the intracranial tension, if prompt, will permit of this formidable danger being excluded.

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[*] **Poggendorff's** 'Annalen der Physik und Chemie,' vol. 80, p. 1, and especially vol. 95, p. 49.

[†] 'Comptes Rendus de l'Académie des Sciences,' vol. 65, 1867, p. 796.

[‡] 'Archiv für Klinische Chirurgie,' vol. 16, 1874, p. 533.

The second remote effect is one which if not so dangerous is as interesting. It consists in more or less extensive hemorrhage at the base of the brain, the extravasated blood filling the sub-arachnoidal space and the sheaths of the cranial nerves. We noticed early in the research that the basal extravasation was not immediately connected with the hemorrhage around the openings of the canal made by the bullet, consequently it was not due to a mere trickling of blood to the base from the vessels torn by the missile. It could therefore only be due to the direct compression at the base at the moment of shot, and produced in the manner discussed on p. 239. That this is so we established by the following experiments. The usual arrangement of the recording apparatus having been made, an abdominal opening was prepared so that, the shot having been fired, a further opening was instantly made in the diaphragm, and the arch of the aorta immediately clamped so as to arrest at a blow the encephalic hemorrhage. The skull was quickly opened and the brain removed. It showed local ecchymosis confined to the track of the bullet and well-marked basal extravasation. Hence, the latter must have been produced at the moment of shot, and in the manner we have indicated.

The sub-arachnoidal hemorrhage just described (especially if combined with intraventricular bleeding) very usually produces oozing of blood, which finds its way down the meninges of the cord, even to the level of the fourth dorsal vertebra. In passing down the cord the blood travels along each side of the ligamentum denticulatum.

Further evidence of the diffuse crushing effect of the missile is afforded by the presence of punctiform hemorrhages in the cortex of the brain, especially where the occipital lobes rest on the bony tentorium, and even where, as on the mesial surfaces of the hemisphere, the brain has been thrust against the falx cerebri. Similar hemorrhages we have observed in the pons, and in various regions of the corona radiata far from the track of the bullet. Such effects are well shown in Fig. 14. Occasionally some hemorrhage may be found in the pia mater and choroid plexus of the fourth ventricle, and this without any hemorrhage into the lumen of the ventricle.

The mechanism of the production of the intraventricular hemorrhages is probably that first described by DURET as "choc céphalo-rachidien," and which consists in the fact that the cerebro-spinal fluid (being incompressible) of necessity transmits directly to the structures of the fourth ventricle any pressure applied to it in the cerebral hemispheres. In the present instance the motion of the bullet produces a direct effect by the energy it imparts to the cerebro-spinal fluid.

CONCLUSIONS.

The following conclusions may be drawn from our experimental results :—

1. That a bullet passing through the cerebral hemispheres immediately produces a

severe elevation of the intracranial tension inducing the state commonly termed compression of the brain.

2. That the primary cause of death in such cases is due not to the failure of the heart, but to arrest of the function of the respiratory centre.

3. That the secondary cause of death is due to hemorrhage and consequently to further elevation of the intra-cranial tension.

4. That the primary cause of death can frequently be removed by the employment of artificial respiration.

5. That the physical influence of the bullet on the encephalic contents is a hydrodynamic one.

APPENDIX.

LIST of Experiments Showing the Path taken by the Bullet.

Experiment.	Bullet.	Path.
1	·38 cal.	Junction of pons and bulb; pons and cerebellum destroyed. Much bruising of upper surface of hemisphere.
2	·38 cal.	Both pre-frontal lobes destroyed. Hemorrhage at base and on 4th ventricle and substance of cerebellar cortex.
3	·38 cal.	Junction of parietal with occipital lobe, and part of cerebellum bruised and left anterior corpus quadrigeminum destroyed.
4	·38 cal.	Left temporo-sphenoidal lobe destroyed and graze of base of brain. No hemorrhage in 4th ventricle. Hemorrhage downwards below 5th cervical nerve.
5	·38 cal.	Entire mesencephalon destroyed. Right lateral lobe of cerebellum shattered. In the pons, cerebellum, and bulb numerous large hemorrhages.
6	·38 cal.	Entire base destroyed. Great laceration of left hemisphere. Bruising of the cerebellum both in its substance and on its surface.
7	·38 cal.	Base and temporo-sphenoidal lobes destroyed. Hemorrhage in membranes of 4th ventricle.
8	·38 cal.	Lower five-sixths of both frontal lobes destroyed. Much bruising of tentorial aspect of cortex. Blood in all the ventricles.
9	·38 cal.	Bullet passed under the left sigmoid gyrus, and destroyed the whole left frontal lobe and sigmoid gyrus. Ventricles free from blood.
10	·22 cal.	Graze of the base of the brain, just anterior to the commencement of the sylvian fissure and of the anterior perforated spot. Blood passed downwards beyond the 7th cervical nerve. None in the ventricle.
11	·22 cal.	Graze of base of brain, just anterior to the sylvian fissure. Both olfactory tracts were destroyed. Much bruising of the cortex at the upper end of the Sylvian fissure. Blood in all the ventricles.
12	·38 cal.	The tips of the frontal lobes and of the olfactory bulbs were destroyed. No blood in the ventricles but hemorrhage in the ependyma of the 4th ventricle.

LIST of Experiments Showing the Path taken by the Bullet—(continued).

Experiment.	Bullet.	Path.
13	·22 cal.	The right frontal lobe, and the sigmoid gyrus, and the left frontal lobe in front of the latter point were destroyed. The olfactory tracts were left. There was notable bruising of the cerebellum and no blood in the 4th ventricle.
14	·38 cal.	The bullet passed through the junction of the frontal and parietal lobes: the former were destroyed.
15	·22 cal.	The bullet track passed through the anterior limit of both occipital lobes, through the corpus callosum and the pineal gland. There was no blood in the aqueduct, but bruising of the 4th ventricle.
16	·22 cal.	The frontal lobes were traversed by the bullet.
17	Saloon pistol, ·22	The bullet passed through the surface of the frontal lobe of the left side only. There was no blood nor bruising.
18	Saloon pistol, ·22	The bullet passed through the parietal lobe just anterior to the Sylvian fissure, *i.e.*, and just below the floor of the lateral ventricle on both sides.
19	Saloon pistol, ·22	The bullet passed through both hemispheres immediately in front of the crucial sulcus, through the coronal sulcus and the corpus callosum.
21	Saloon pistol, ·22	The bullet passed through the parietal portion of the hemisphere just anterior to the plane of the external auditory meatus, *i.e.*, exactly through the upper end of the Sylvian fissure. There was much hemorrhage at the base, and none in the ventricles.
22	Saloon pistol, ·22	The olfactory lobes and tracts were destroyed. There was hemorrhage around the cord, and slight bruising in the 4th ventricle.
23	Saloon pistol, ·22	The aperture of entry was opposite the left crucial sulcus: the aperture of exit was 1·5 centims. behind the Sylvian fissure. The track of the bullet was immediately above the corpus callosum.
24	Saloon pistol, ·22	The bullet passed through the brain just below the outer extremity of the crucial sulcus, through the coronal sulcus, through both hemispheres obliquely forward, and so through the corona radiata, just in front of the ventricles. There was much hemorrhage at the base.
25	Saloon pistol, ·22	The bullet passed both parietal lobes, entering on the left side, just in front of the upper end of the Sylvian fissure. The exit was through the upper border of the coronal gyrus in the plane of the crucial sulcus. There was a minute bruise on the left side of the 4th ventricle. There was no blood in the 4th ventricle, but some in the lateral ventricle.
26	Saloon pistol, ·22	A grooving shot through the centre of the upper fifth of both hemispheres, far above the corpus callosum. There was no blood in the ventricle, but bruising in the lateral lobe of the cerebellum and 4th ventricle, especially on the right side.
27	Saloon pistol, ·22	The left cortex was grooved along the pre-crucial gyrus, and the right post-crucial gyrus was just grazed. There was slight symmetrical bruising in the lateral lobe of the cerebellum and none in the ventricles. There was blood in the meninges on the side of the left hemisphere but none at the base.
28	Saloon pistol, ·22	The bullet entered the left hemisphere just at the outer end of the crucial sulcus, passing out anteriorly and inferiorly to the sigmoid gyrus on the right side, through the prorean sulcus. There was slight hemorrhage round the medulla, and under and around the cerebellum and mesencephalon, none in the 4th ventricle, and very slight at the base.

List of Experiments Showing the Path taken by the Bullet—(continued).

Experiment.	Bullet.	Path.
30	Saloon pistol, ·22	The bullet passed through the olfactory lobe. There was much hemorrhage at the base of the pons, and posteriorly over the right occipital lobe and the surface of the cerebellum. There was none in the ventricle, though great hemorrhage round the medulla.
31	Saloon pistol, ·22	The entry was just in front of the Sylvian fissure. The corpus callosum was traversed. There was no blood in the aqueduct but great hemorrhage round the medulla.
32	Saloon pistol, ·22	The bullet passed through the olfactory lobes. There was scarcely any bruising externally, except slight along the optic tracts, elsewhere there was none.
33	Saloon pistol, ·22	The bullet passed through the hemispheres in the plane of the Sylvian fissure. There was much bruising of the vertex of the left hemisphere, but little of the right. There was no hemorrhage in the ventricles, but they were all bruised, while there was slight basal hemorrhage.
34	Saloon pistol, ·22	The passage of the bullet was through the parietal lobes, just in front of the left Sylvian fissure, and through the upper end of the right Sylvian fissure. There was much basilar hemorrhage in the arachnoid and round the bulb. There was no hemorrhage in the posterior cornu of the lateral ventricle, but great bruising and hemorrhage of the fissure of Bichat, and in the lower half of the 4th ventricle. There were also hemorrhages in the lateral lobe of the cerebellum.
35	Saloon pistol, ·22	The bullet entered at the outer extremity of the left crucial sulcus, and passed diagonally through the brain, leaving the hemispheres through the temporal lobe. There was notable bruising but no hemorrhage in the 4th ventricle, and there was but slight basilar hemorrhage.
36	Saloon pistol, ·22	The bullet passed through both olfactory tracts and tips of the frontal lobes. The ventricles were free from blood, but there was slight bruising throughout the left hemisphere, though none in the right.
38	Saloon pistol, ·22	The bullet passed through the fronto-temporal suture, *i.e.*, just in front of the Sylvian fissure, through the right Sylvian fissure. There was hemorrhage at the exit in the meninges, and hemorrhage and bruising in the lateral ventricle.
39	Saloon pistol, ·22	The first shot caused a slightly depressed fracture of the coronal suture, with slight bruising of the brain beneath. The second bullet traversed the left occipital lobe, the corpora quadrigemina, and the fissure of Bichat.
40	Saloon pistol, ·22	The bullet entered the coronal sulcus just below the post-crucial gyrus. Bruising present in the 4th ventricle, but no hemorrhage, although much had occurred at the base of the bulb.
41	Saloon pistol, ·22	The bullet entered just below and behind the left crucial sulcus, between it and the upper end of the Sylvian fissure, and passed through the brain by an exit through the right temporal lobe just below and behind the Sylvian fissure. There was slight hemorrhage at the base of the left side and notable bruising, but no hemorrhage in the 4th ventricle.
42	Saloon pistol, ·22	The bullet passed through the brain just behind the sigmoid gyrus, and on a level with the corpus callosum. There was much bruising in the left lateral ventricle and well marked in the 4th ventricle. There was moderate hemorrhage at the base.
43	Saloon pistol, ·22	The bullet just penetrated the dura, bruising the brain immediately in front of the crucial sulcus, the bone being driven into the hemisphere. There was no other lesion.

List of Experiments Showing the Path taken by the Bullet—(continued).

Experiment.	Bullet.	Path.
44	Saloon pistol, ·22	The bullet passed through both hemispheres just below and behind the sigmoid gyrus, opening both lateral ventricles. Much general bruising of the vertices, moderate bruising at the base, and bruising of the left half of the aqueduct and of the passage of the 4th ventricle.
45	Saloon pistol, ·22	The bullet entered the left hemisphere just below and posterior to the left sigmoid gyrus, cutting the corpus callosum.
46	Saloon pistol, ·22	The bullet entered just through the foot of the pre-central gyrus, and passed downwards with an exit through the right Sylvian fissure. There was moderate hemorrhage at the base, but not in the 4th ventricle, nor in the longitudinal fissure.
47	Saloon pistol, ·22	The first shot did not penetrate, and only caused a small very superficial bruise, 1 centim. below the outer margin of the left gyrus. The second shot passed through the hemispheres on a level with the upper end of the left Sylvian fissure, and the lower end of the right Sylvian fissure. There was bruising and hemorrhage of both ventricles. Very slight bruising of the 4th ventricle, and moderate hemorrhage on the left side of the base.
48	Saloon pistol, ·22	The bullet penetrated the base of the brain close to the optic chiasma. There was no hemorrhage in the rest of the base and only slight bruising of the 4th ventricle.
49	Saloon pistol, ·22	The bullet perforated both hemispheres through the posterior angle of the sigmoid gyrus. The brain was large and there was no effect in the ventricle or the base.
50	Saloon pistol, ·22	The bullet entered the left hemisphere through the cornu sulcus, opposite the crucial sulcus, through the top of the right Sylvian fissure 1 centim. below the point of entry. There was moderate hemorrhage at the base chiefly on the left side. Nothing in the 4th ventricle.
51	Saloon pistol, ·22	The bullet passed through the hemisphere immediately between the sigmoid gyrus and the top of the Sylvian fissure passing above the corpus callosum. There was moderate hemorrhage under the bulb.
52	Saloon pistol, ·22	The bullet passed through the left occipital lobe just behind the upper end of the Sylvian fissure. It left by the fissure of Bichat, grooving the right occipital lobe. There was slight hemorrhage at the base.
53	Saloon pistol, ·22	Both anterior lobes totally destroyed.
54	Saloon pistol, ·22	Both occipital tracts and bulbs destroyed. Much hemorrhage and laceration at the base. Much bruising in the 4th ventricle and lateral ventricle, but not hemorrhage.
59	Saloon pistol, ·22	The bullet entered between the sigmoid gyrus and the upper end of the Sylvian fissure and traversed both hemispheres, causing some bruising of the 4th ventricle and hemorrhage and bruising of the lateral ventricles.
60	Saloon pistol, ·22	The bullet traversed both Sylvian fissures. There was much hemorrhage at the base and round the medulla. There was also much bruising in the ventricle, and hemorrhage only in the track.
61	Saloon pistol, ·22	The bullet was found lying on the velum just behind the foramen of Munro. There was no hemorrhage in the ventricles but some slight bruising.
62	Saloon pistol, ·22	The bullet passed through both hemispheres just behind the top of the Sylvian fissure. There was slight hemorrhage at the base and much bruising in the ventricles but no hemorrhage.

List of Experiments Showing the Path taken by the Bullet—(continued).

Experiment.	Bullet.	Path.
63	Saloon pistol, ·22	The bullet passed through the left cerebral hemisphere, just in front of the upper end of the Sylvian fissure and out just behind the upper end of the same. There was slight hemorrhage at the base, also much bruising in the lateral ventricles, especially the left, and very slight hemorrhage in the 4th ventricle.
64	Saloon pistol, ·22	The first shot penetrated both marginal gyri. In the second shot the bullet passed through a point 2 centims. below the former.
65	Saloon pistol, ·22	Cortex of right hemisphere completely destroyed.
66	Saloon pistol, ·22	The skull was opened. The bullet entered through the left occipital lobe, and passed diagonally downwards through the cerebellum.
67	Saloon pistol, ·22	The skull was opened. The first shot passed through the frontal bone and lobe. The second shot passed through the exposed occipital lobe, and the third shot through the 4th ventricle.

DESCRIPTION OF PLATE 3.

Fig. 1. Ammunition employed; actual size.

Fig. 2. Photo. of brain (Experiment 2). The bullet traversed the præfrontal region, but nevertheless caused extensive bruising of the tentorial surface of the occipito-temporal region of both hemispheres, of the cerebellar hemispheres, and in the membranes of the 4th ventricle.

Fig. 3. Photo. of preparation showing longitudinal expulsion of brain through an opening in the skull by bullet passing at right angles to longitudinal axis of cranial cavity. *a*, aperture of entry of bullet; *b*, thick edge of opening in bone; *c*, finger-like portion of occipital lobe forced 1·8 centim. out of the opening (which in this case was 1 centim. in diameter).

Fig. 4. Example of KOCHER'S experiment.

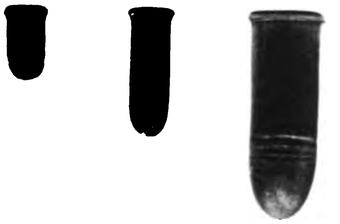

Fig. 1.

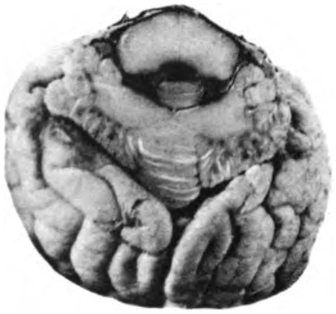

Fig 2.

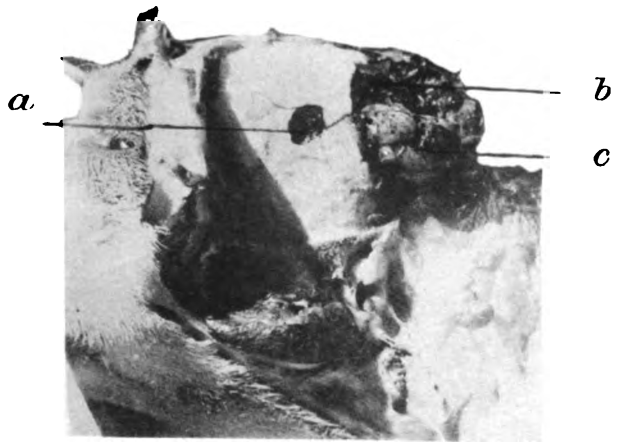

Fig. 3.

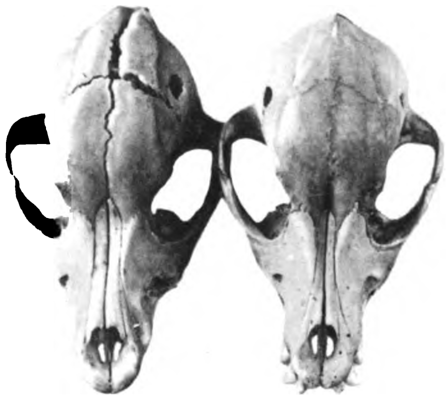

Fig. 4.

VIII. *On the Regeneration of Nerves.*

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[PLATES 4–9.]

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I.—HISTORICAL INTRODUCTION.

THE view expressed by GALEN that nerves once divided are incapable of undergoing repair, was that universally accepted until the latter part of last century. It is true that GUY DE CHAULIAC* speaks of the perfect restoration of divided nerves, but as he speaks at once of nerves and tendons, it is doubtful whether we can accept his remarks as really referring to nerves.

CRUIKSHANK (2) was the first to show that reunion is possible. He divided the vagus of the right side in a dog, and three weeks later excised a portion from the nerve of the opposite side, and the animal made a perfect recovery. Three weeks later he killed the dog, and found both nerves reunited. The results of his investigations were communicated to the Royal Society on 13th June, 1776, but his paper was not printed until nineteen years later. His preparation, however, was placed in WM. HUNTER's Museum, and was the means of stimulating others to further researches. I found this preparation in the Museum in Glasgow University, and was easily able to identify it from the drawing published with the paper.†

CRUIKSHANK himself held on physiological grounds that the nerves in his preparation were united by nerve substance, but the prevailing opinion was that the bond of union was composed of connective tissue. FONTANA (3), MICHAELIS, HAIGHTON (6), MEYER (7), and PRÉVOST (10), supported the former view, on the ground of their own researches, while MONRO (4), ARNEMANN (5), and others held to the latter view. The work of STEINRÜCK (14) which appeared in 1838, set the matter at rest, for from that time the possibility of reunion of nerves by nerve substance is admitted by almost all observers.

With NASSE (15) a new field of investigation was begun, for that observer discovered that after section of a nerve, degeneration of the primitive fibres occurs. He, however, only examined the seat of section, as also did GÜNTHER and SCHÖN (16) in the following year, and STANNIUS (18) a few years later, while he observed on one occasion degeneration of the ultimate ramifications of the nerve in the muscular fibres after section of the stem, did not follow up the clue, but left to WALLER (20, 22 to 29) the discovery of the inevitable degeneration of the whole peripheral segment after section of a nerve, and the enunciation of the law of dependence of the nerves for their nutrition on trophic centres. WALLER's view is that after section of a nerve, the whole nerve fibre is destroyed, and that it never can recover its structural characters or functional properties, and that the young nerve fibres are new formed structures

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* GUIDO DE CAULIACO (1), p. 114, "Ego vidi et audivi in multis nervos et thenanton incisos; et eos ita restauratos cum sutura et aliis auxiliis, quod erat postea incredibile ipsos fuisse incisos."

The numbers in parenthesis refer to the Bibliography, p. 287.

† My thanks are due to Professor YOUNG for granting every facility for and help in identifying this preparation. The delay in printing CRUIKSHANK's communication until after the death of HUNTER accounts for the history of the preparation not having been inserted in the Catalogue of the Museum.

always found lying between the old degenerated remains; that they are never found till reunion has occurred; and that they start in the intermediary uniting segment, and travel on to the ultimate ramifications of the nerve.

This view was widely accepted, but the length of time required for such a process of regeneration was found not to accord with clinical observations made by **Paget** (30), and experimental observations by **Schiff** (31) and by **Bruch** (32), and these observers held that nerves must also be capable of undergoing repair by first intention, to account for the rapid return of function, which they found after certain cases of nerve section.

The view advanced by **Waller** that the peripheral segment of a divided nerve is incapable of being regenerated, until reunited to the central segment, had been received without contradiction. **Philipeaux** and **Vulpian** (38, 39), however, while corroborating the ultimate degeneration as a result of separation of a nerve from its centres, found that the peripheral segment can, even while remaining separate from the central segment, undergo reparation. Not only so, but a portion of the lingual nerve transplanted under the skin of the inguinal region in dogs contained new fibres after six months (47). These observers held that the axis-cylinder was not destroyed during degeneration, and that restitution consisted simply in a reaccumulation of the myeline, and that, therefore, restitution was simply a restoration. Their results were met by much opposition, **Schiff** (41), **Landry** (42), and **Ambrosoli** (43) writing at the time in opposition to them, and since, almost all the writers have opposed their conclusions, some maintaining with **Ranvier** (102) that the regeneration which they observed was due to connecting strands of tissue between the proximal and distal ends, strands which they had failed to observe, and even **Vulpian** (77, 86) himself, some years later, withdrew from his former position, admitted that what had been seen were not regenerated fibres, and denied the possibility of autogenetic regeneration of nerves. Their conclusions, however, are supported by **Mitchell** (80), and more recently by **Bowlby** (146).

The general opinion was against the possibility of reunion of nerves by first intention, when in 1864 the cases of nerve suture in man by **Nélaton** (54), and **Laugier** (55) were published. In **Nélaton**'s case a neuroma was excised from the median in the arm, and return of function was established in a few days, and in **Laugier**'s case the median was completely divided in the forearm, was sutured, and function returned in a few days.

The interest in the subject of nerve regeneration was greatly increased by the publication of these cases, and several workers were induced to commence experimental research to investigate the matter. **Eulenburg** and **Landois** (56, 60), from their investigations in animals, strongly opposed the view that nerves could heal by first intention, and thought the employment of suture a highly dangerous proceeding. **Magnien** (61), on the other hand, found no harm from the employment of suture, and in two cats he found return of function in a few days after section and employment of suture.

Further doubt was thrown on the value of the clinical experience of early return of function after nerve suture, by the experiences of **Richet** (62) and of **Létiévant** (73, 82). **Richet** observed a case in which, after section of the median nerve, sensation remained in the distribution of that nerve; and **Arloing** and **Tripier** (70) explained the case by showing that in the dog there is in the skin an anastomosing network of the ultimate fibrils of all the nerves supplying the paw, and that no part of the skin is exclusively supplied by a single nerve. **Létiévant**, again, found that after section of the median nerve without reunion, movements were developed in the hand which resembled those performed by the muscles supplied by the divided nerve, and showed that these movements were imitations by neighbouring muscles, whose supply remained intact, of the movements performed by the paralysed muscles. He also showed that, though the sensory supply of a region is cut off, sense of touch may remain by mediate communication with other nerves. **Tillmanns** (123), again, supposes that from neighbouring intact nerves, filaments may grow out into the anæsthetic region; and **Remak** (87), that anastomosing fibres may develop after nerve section, in a way comparable to the development of the collateral circulation after occlusion of an artery.

Thus the clinical experience of early return of sensation after nerve section has been discredited as a proof of the reunion of the nerve. **Vanlair** (122), for example, considers that if after nerve section sensation returns in a very short time, it is due to anastomosing fibres, and the short period of anæsthesia is due to the numbing effects of hæmorrhage; if more slowly, that it is due to supplementary supply; and that if a very long time elapses, then it is due to regeneration of the divided nerve.

But the cases of secondary suture published speak strongly against the slow process of regeneration from the central end. One of the first of these was a case published by **Jessop** (75), where the ulnar nerve had been cut across above the wrist nine years before the operation of suture. Before the operation there was total loss of sensation and motion in the region supplied by the ulnar. The hand was thin and the palm hollowed out. The cicatrix uniting the ends was excised and the nerve sutured, and eight days after the operation sensation began to return, and in eight days more had returned everywhere, except at the tips of the fingers. A similar case was published by **Langenbeck**.* In his case the sciatic had been cut across two and a half years before the operation, and there was total anæsthesia, and yet sensation began to return three days after the operation. Also **Ogston** (120) performed secondary suture of the ulnar in a case in which the nerve had been cut long enough to produce the characteristic atrophy and claw-hand, and in which there was total loss of sensation and motion, and yet, a week after the operation, the return of sensation was determined.

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* After **Wolberg** (127), p. 341.

These and similar cases in which sensation remains totally lost before operation and long after the date of section of the nerve, but returns in a few days after the operation, cannot be explained on the theories mentioned, and must indicate a reunion of the nerve, and re-establishment of conductivity; and these cases would indicate that nerves, though long divided, must be capable of very early reunion, when placed in suitable conditions for that to take place.

At present the views of the histological process of regeneration are divisible into two groups:—

1st. The view established by RANVIER (81,102), and closely coinciding with that of WALLER, that the peripheral segment of the nerve takes no part in the process of regeneration, but that the latter is effected entirely by growth of new axis-cylinders from those of the central end of the nerve, the peripheral segment acting merely as a guide for growth to the end organs. This view is very widely accepted, and is supported by the histogenetic researches of KÖLLIKER (109) and HIS (111, 144, 147). It has been recently supported by HOWELL and HUBER (156), STROEBE (158), and NOTTHAFFT (159), who, however, find that the envelopes of the axis-cylinders are supplied from elements in the peripheral segment.

2nd. The view that the new fibres are derived from elements in the distal segment, and that the young fibres thus formed become attached to the fibres of the central segment, and thus restore conductivity. Recently BÜNGNER (150) has adopted this view, and holds that the young fibres are derived from the protoplasm and nuclei of the interannular segments. These form spindle-cells which unite end to end, and form protoplasmic threads, which soon show longitudinal striation, the beginning of the axis-cylinder. The new myeline sheath is formed from the outer layer of the young fibres, and also partly by absorption of the old myeline. The old sheath of SCHWANN disappears, and the new is derived from the endoneurial tissue. The nuclei of the new sheath of SCHWANN, are the direct descendants of the nuclei of the old, and have clearly the value of neuroblasts. This view coincides with the histogenetic researches of BALFOUR (93, 121) and MILNES MARSHALL (97).

According to the first view, the process of regeneration requires for its accomplishment a more or less long period of time, depending on the length of the peripheral segment. Thus VANLAIR (160) estimates the rate of growth from the central end to be from 0·3 millim. to 1 millim. daily, after section and immediate perfect coaptation. According to the second view, the time is not necessarily long, seeing that the material for the work of regeneration is already laid down along the whole length of the peripheral segment. Thus the published cases of secondary suture, with speedy return of sensation, are enigmatical on the first view, but are capable of explanation on the second view.

II.—CASES OF SECONDARY SUTURE OF NERVES.

My observations were made on four cases,* in three of which the nerves had been accidentally divided some time previously, and functional reunion had not occurred; while in one the nerves were functionally interrupted by compression at the seat of a fracture. The cases were as follows:—

Case I.—Division of the ulnar and median nerves in the forearm.

Case II.—Division of the median nerve in the forearm.

Case III.—Interruption of the median, ulnar, and musculo-spiral nerves, resulting from a fracture at the elbow joint.

Case IV.—Division of the ulnar nerve in the forearm.

These cases, therefore, presented seven injured nerves. In the cases of division, I performed the operation of secondary suture, and in that of compression at the seat of fracture, dissected the nerves from their adhesions, and removed the compressed portions from the median and musculo-spiral, and sutured. In every case the portions removed were preserved for microscopical study.

Case I. (Plate 4, figs. 1 and 2.)

A boy, aged 16 years, received a wound with a piece of glass, on the front of the right forearm in its middle third. The wound was deep, and bled freely. It was sutured, and healed in about eight weeks, but by that time it was apparent that damage had been done to the nerves, as the hand was paralysed and sensation lost. Soon atrophy manifested itself, and the boy was unable to return to his work. He came for advice on 3rd March, 1894, fully six months after the accident, and his condition was found to be as follows:—

A cicatrix, 13 centims. in length, extended across the middle third of the front of the right forearm, obliquely from above downwards and inwards, crossing almost the entire breadth of the forearm. The lower and inner third of this cicatrix was red, and painful when firmly pressed; the middle third was extremely red, and prominent at its junction with the inner third, and its surface was thin and very tender even to the slightest touch; the upper and outer third had the appearance of an ordinary cicatrix. On moving the fingers, the cicatrix was found adherent to the muscles. The muscles of the forearm were atrophied, the right forearm being everywhere about 1 centim. less in circumference than the left at corresponding levels.

The trophic changes in the hand were well established. The skin was smooth red, and shining, and the flexures but little marked. There was a raw surface, without signs of healing, on the inner side of the first internode of the fifth digit;

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* I owe to DR. PATTERSON my sincere thanks for permission to perform these operations in his ward in the Western Infirmary, Glasgow, and also for valued suggestions thereon.

this was the result of a burn received two weeks previously. The nails had a corrugated surface. The hand was colder than the left. There was great atrophy of the small muscles, the palm being hollowed out and the thenar and hypothenar eminences replaced by hollows.

The attitude and movements of the hand were those characteristic of section of the median and ulnar nerves. Thus all the fingers were held flexed at the two interphalangeal, and overextended at the metacarpo-phalangeal joints. The fingers could be passively extended, but voluntarily only to a slight extent, and in both cases only with accompanying flexion of the hand at the wrist. The hand was carried semiflexed at the wrist, simulating wrist-drop, but could be voluntarily straightened, although it could not long be held in that position, as a painful feeling was soon developed. He could also perform lateral movements of the hand at the wrist. The hand could only be partially closed, and when he attempted to extend his fingers keeping the wrist straight, only the first phalanges responded, the two distal remaining flexed. The movements of adduction and opposition of the thumb, and abduction of the fingers were impossible. With the hand dynamometer, he registered with the right hand 4 kilos., and with the left 16 kilos. The small muscles of the hand tested electrically gave no response to the faradic current, but responded to the galvanic current.

The condition of sensation was as follows. There was pain elicited by pressure over the terminal phalanx of the thumb; absolute anæsthesia, even for touch, in every part of the fifth and fourth digits; very slight sensation, but none for pain, as tested by pricking the skin with a pin, on the third digit and palmar aspects of the second and first; total anæsthesia of the palm and of the ulnar side of the dorsum of the hand; and normal sensation on the radial side of the dorsum of the hand, and over the thenar eminence and dorsal aspects of the first and second digits.

On 15th March, 1894, exactly six and a half months after the accident, I performed the operation of secondary suture. The median nerve was laid bare at the seat of section, and the two ends of the nerve were found united by a dense cicatricial mass, somewhat thicker than the nerve, and about 1·5 centim. in length. This cicatricial mass lay under the middle third of the skin cicatrix, which was found at the examination to be so very tender. The nerve itself was much thicker than a normal median nerve.

The ulnar nerve was next exposed through the same incision. It was found similarly hypertrophied, but the ends were separated about.2 centims. The central end lay about the level of the tender inner and lower third of the cutaneous cicatrix, and presented a hard bulb measuring about 1·5 centim. in length and 1 centim. in transverse diameter. The peripheral end lay at a lower level than the cicatrix in the skin, was not so much hypertrophied, and presented a bulb about half the size of that on the central end. It lay surrounded by loose connective tissue.

The cicatrix on the median was excised at its junction with the ends of the nerve, and while the surface exposed at the central end showed nerve substance, that on the peripheral presented a homogeneous aspect. On removing an additional slice from the latter, nerve substance was exposed, and the section presented an appearance similar to that of the central end. The bulb on the central end of the ulnar was then cut off, and then the smaller bulb from the peripheral end, the sections in both cases exposing nerve tissue. Two sutures of chromic catgut were passed through each of the nerve ends by means of a flat needle, the plane of the needle being kept parallel to the course of the nerve fibres in order to inflict as little damage as possible. The hand and forearm were then fully flexed, and the sutures tied. The median came together easily, but the ulnar ends could not be brought together nearer than about 6 millims. The forearm and hand were then fixed fully flexed in a splint.

Three days after the operation, the first sign of returning sensation appeared; for on pinching the tip of the little finger, while the patient's head was covered, he cried out with pain. On the following day, he recognised the little finger when touched, and felt pain when it was firmly grasped or pricked with a pin. On the ninth day, the wound was dressed for the first time, and the patient stated that he felt his hand much stronger than before the operation. The improvement in sensation was maintained. On the nineteenth day, relaxation of the extreme flexion was begun gradually, and a more careful examination made of the condition of sensation. It was then found that he localised correctly all parts of the fingers touched, unless when the touches were slight, when he occasionally mistook the finger touched, and occasionally failed to feel a gentle touch on the little finger. The sore on the first internode of the little finger was now quite healed, and the operation wound was healed, except at the extreme ends, through which drainage had been made. Towards the end of the first month, the sensation had still further improved; for now he located correctly the gentlest touches, and responded quicker than he did at first. The limb had now been gradually extended, and the fingers, also, had now been fully extended by firm bandaging to the splint. He could also at this time partially close and again open the hand. Electrical treatment of the hand was then commenced. With the positive pole applied above the wrist over the respective nerves, and the negative to ZIEMSSEN's points over the small muscles, there were no contractions with the faradic current, but with a moderate galvanic current there were distinct contractions of the small muscles of the thumb; but only very slight contractions could be detected in the other small muscles. By a month and a half from the date of operation, the electrical condition had improved; for now, while all the small muscles responded to the galvanic current, the small muscles of the thumb gave contractions with the faradic current. There was also a notable return of power in the hand, as his grasp was appreciable. He was able to write legibly, which he was quite unable to do before the operation. By two months, the appearance of the skin had improved, and he was able to open and close the hand; but beyond a slight degree he could not oppose the thumb. The cicatrix of the original wound, which was so red and tender before the operation, had now the appearance of an ordinary cicatrix, and had lost its tenderness. In the fifth month, he stated that he found no difference in sensation between the two hands, and that the hand was useful, although he was still unable to perform the more delicate movements; and this was explained by the persistent weakness of the opponens pollicis muscle. Despite the improvement in power, the atrophy of the palm and of the thenar and hypothenar eminences was still distinct, though less. The patient was last seen seven months after the operation, and at that time the improvement in sensation and motion was maintained, and the grasp of the hand much stronger. The sensation of the hand was perfect, and the appearance of the skin much improved; but there was still marked atrophy of the small muscles. The improvement in grasp up to that time is shown in the following table, taken with the hand dynamometer:—

Date.		Right.	Left.
		kilos.	kilos.
March 3 . . .	Before operation	4	16
„ 15 . . .	Operation		
May 1	. . . .	2	
„ 8	. . . .	4	
„ 16 . . .	. . . .	7	
June 21 . . .	. . . .	8	16
October 19 . .	. . . .	14	29

Case II.

A man, 37 years of age, a carpenter, on 20th November, 1894, received a deep wound with a chisel on the right forearm, transversely, just above the wrist in front. The wound was not stitched, and was said to have healed in about a fortnight without suppuration. Immediately after the accident he noticed loss of sensation in the thumb and index and middle fingers. Sensation did not return, and the hand being useless, he sought advice on 28th February, 1895. His condition then, three months and eight days after the accident, was as follows:—

On the right forearm there was a linear cicatrix, 2·5 centims. in length, situated transversely above the wrist in front. Through this cicatrix a dense oval swelling, about the size of an almond, could be felt in the middle line of the forearm, and on applying pressure a tingling sensation shot up the arm and down into the hand. The skin, especially of the front of the index finger, thumb, and outer half of the palm, was smoother than is natural, and the flexures were greatly diminished. There was marked atrophy of the thenar eminence. The index and middle fingers could not be fully extended, nor could they be brought into contact with the palm; and there was considerable loss of power of flexion of the thumb, and the movement of opposition was impossible.

The condition of sensation was the following:—Total anæsthesia on the anterior aspects of the thumb, index, and middle fingers, and on the outer half of the palm; only obtuse tactile sensation on the outer side of the ring finger and over the thenar eminence. On pricking with a pin the palmar surfaces of the thumb, index, middle, and outer half of the ring fingers, no pain or other sensation was felt.

On 28th February, 1895, the median nerve was exposed by a longitudinal incision, 5 centims. in length, over the seat of injury. The nerve was found hypertrophied, and the ends united by a dense mass of cicatricial tissue, about 2 centims. in length and 1·5 centim. in greatest breadth, but flattened antero-posteriorly. This mass was excised at its junction with the nerve, and the sections exposed at the ends of the nerve showed points of what appeared to be nerve substance, but these were separated by dense white tissue. Two sutures of chromic catgut were passed through the whole thickness of the nerve, and the ends drawn together, and this was easily effected when the hand was fully flexed. The wound was closed, and no drainage used, and the limb bandaged to a splint with the hand fully flexed.

Two days after the operation sensation commenced to return. The sense of touch was present on the palmar aspects of the fingers and thumb, and a pin thrust into the palmar aspect of the thumb was felt as a painful sensation; but sensation was still vague. By the ninth day sensation was much improved, and by the thirteenth day pain was felt from the prick of a pin in the palmar aspects of all the affected fingers and in the thumb, and by the seventeenth day there was still further improvement. From this time the hand was gradually relaxed, and, finally, about the fourth week, when got into the extended position, the splint was discarded. A fortnight later there was distinct improvement in the muscular power of the hand. Towards the end of the second month (24th May) his sensation had further improved, and both touch and sense of pain were quite distinct, although not yet felt by the patient so distinct as in the other hand, but the point of the index finger was not so sensitive as the other parts of the median distribution. The improvement in the muscles was very decided; for not only had the atrophy of the thenar eminence in great part disappeared, but the movement of opposition was now so well developed that he was able to touch the tip of the middle finger with the tip of the thumb. At the end of six months, there was still further progress. Localisation of touch was perfect for all the parts concerned, and there was much improvement in the sensation of the last phalanx of the index finger; but even yet the patient found sensation less acute than in the sound hand. The grasp was almost as good as that of the left hand, and the movement of opposition was still further improved, since now he could touch with the thumb the tip of the ring finger. What prevented him from having as perfect use of his hand as formerly, was his inability to flex completely the terminal phalanges of the index and middle fingers. Thus, when he closed his hand, the tips of these fingers did not come sufficiently into the centre of the palm to enable him to grasp firmly smaller objects; but for larger objects his grasp was as firm as that of any average hand. He had already some time since returned to his work, being able to use his hand. At the end of nine months the condition was further improved. He could distinguish with each finger the difference between the smooth and rough side of sand-paper. The atrophy of the thenar eminence had not only disappeared, but the eminence was even slightly greater than that of the left hand, and he was able to pick up the smallest piece of paper between fingers and thumb, although at six months he could only pick up a coin. At the end of a year, there was still further improvement, as he could now oppose the thumb to the little finger, but the grasp for smaller objects was still defective from his inability to flex completely the terminal phalanges of the index and middle fingers, although it was better than at nine months. His sensations of touch, pain, and thermic difference were correct, although not felt quite so clearly as in the left hand. As showing the degree to which the grasp had improved compared with that of the left hand, the dynanometer reading is of importance. One year and four months after the operation, with the right hand he registered 54 kilos., and with the left 58 kilos. (Plate 5, figs. 1 and 2.)

Case III. (Plate 6, figs. 1 and 2.)

A girl, aged 6 years, sustained a fracture of the left elbow joint from a fall. The limb was fixed in splints, which were removed at the end of four weeks. Her hand was then found to be anæsthetic and paralysed. On 12th December, 1895, eight weeks after the accident, I first saw her, and found her condition to be as follows :—

The internal condyle at the elbow joint was thickened, but otherwise the appearance of the joint was normal. The joint, however, only permitted a slight range of voluntary movement, and even under chloroform this range could not be much increased on forcible passive movement. The child carried the forearm flexed at a right angle, and the supinator longus was felt firmly contracted. Supination and pronation could not be voluntarily performed, but were easily accomplished passively. The hand was carried flexed, and could not be straightened, its range of movement being very limited. Voluntary motion was abolished. The first phalanges of the fingers were extended; the second and terminal, flexed. The first phalanx of the thumb was extended; the terminal, flexed. By passive movement the two distal phalanges of the fingers could be extended, only when the first were flexed. The forearm was wasted only to a degree appreciable by measurement; but the hand showed distinct trophic changes. Thus the dorsum was unnaturally smooth and wasted, and on the palmar aspect, and especially at the tips of the fingers, the skin was smooth and glossy, and on the palm the flexures were very indistinct. The small muscles were atrophied, giving a scooped-out palm, and hollows in place of the thenar and hypothenar eminences. Voluntary movement of the fingers was scarcely appreciable, but the slightest degree of flexion and extension could be detected.

With the faradic current the muscles of the forearm and hand gave no response; but with the galvanic, good contractions. Sensation in the forearm was normal; but neither touch nor the prick of a pin could be felt in any part of the hand, except over the outside of the first metacarpal bone, extending over the thenar eminence for a short distance in a less distinct degree.

On 13th December, 1895, the musculo-spiral nerve was exposed by an incision about 9 centims. in length, crossing the bend of the elbow. The nerve exposed to view was much thickened, and, a little below the bend of the elbow, where it divides into radial and posterior interosseous, it was firmly bound down by, and adherent to cicatricial tissue. This nerve exposed, the wound was temporarily closed, and the elbow joint then excised through a single incision behind. The ulnar nerve was next laid bare from the deep surface of the internal flap. The ulnar was also considerably hypertrophied, and firmly adherent at the level of the joint. It was freed from its adhesions. The median nerve was then exposed by an incision in front. It also was hypertrophied, and firmly adherent to the surrounding cicatricial tissue. It was dissected from its adhesions, but these being very intimate, the portion which seemed to be most involved was excised, that portion measuring about 12 millims. in length. The ends were then brought into apposition, which was easily effected after the excision of the elbow joint, and sutured with two chromic catgut sutures, passed through the whole thickness of the nerve. The musculo-spiral was then dissected from its adhesions, and as these were very intimate at its point of bifurcation into its two branches, the radial was divided about 6 millims. from its origin and the posterior interosseous about 3 millims. from its origin. The terminal portion of the musculo-spiral was then removed about 12 millims. from its bifurcation, and the two peripheral ends united to the central end of the musculo-spiral with chromic catgut. The wounds were then washed and sutured and drained with catgut. The limb was then fixed in a splint with the forearm semi-bent.

The dorsum of the hand, the only part exposed, was tested daily for the first sign of returning sensation; but there was no change till the fourth morning after the operation, when there was an indication of improvement, in so far that some sensation, produced by pricking with a pin, was found extending downwards from the wrist, but only for a short distance. There was no further change till the seventh day, when the sensation had travelled down to the level of the mid-transverse line on the dorsum of the hand. There was also a point on the inside which was sensitive. On the following day there was sensation on the inside as far as the head of the metacarpal bone, and also a further extension on the outside. Pricking the skin of the palm with a pin caused the child to cry with pain. On the ninth day the same conditions obtained, but the child could as a rule locate the region pricked, but occasionally made a mistake. On the eleventh day there was obscure sensation in the fingers. The improvement continued, and on the seventeenth day the wounds were dressed and found healed, except at the points where they had been drained. The arm was put on a rectangular splint, and the fingers bandaged out straight. The sensation had now so far improved, that the child could locate the finger pinched, although occasionally she made a mistake. At the end of six weeks, the last occasion upon which the patient was seen, the sense of pain on being pricked with a pin had returned in the little finger, and was quite distinct in the palm, but the other regions of the hand were still insensitive to pain. There was no return of motion, and the electrical reactions remained as before the operation.

Case IV. (Plate 5, fig. 3.)

A woman, aged 29 years, sustained a cut with a piece of glass on the right forearm, about 2·5 centims. above the wrist, extending from the front round the inside. The wound was stitched and healed without trouble, but she soon discovered that she had lost sensation in the little and ring fingers. Shortly afterwards the little and ring fingers and the palm of the hand began to waste, and the skin to assume a smooth glossy appearance. I saw her for the first time on 23rd January, 1896, eighteen months after the accident, when she presented the following condition:—

The position of the wound was marked by a linear cicatrix on the right forearm commencing near the middle line in front, 2·5 centims. above the wrist, and extending inwards to the ulnar side, curving upwards in its course. The cicatrix was not tender, but when firmly pressed, a tingling sensation was sent up the arm and down into the hand. The little and ring fingers were over-extended at the metacarpo-phalangeal joints, and semi-flexed at the first and second interphalangeal joints. Both fingers were smooth and glossy, the ring finger showing these characters more so on its inner side. The inner half or three-quarters of the palm had a similar shining appearance, and the flexures had almost disappeared. The nail of the little finger was rough and irregularly grown. The joints of the two affected fingers were stiff, and allowed only a limited range of movement either voluntary or passive. The two inner fingers could not be brought into contact with the palm, when she attempted to firmly close the hand. There was both on the little finger and inside of the ring finger, and on the inner half of the palm some slight sensation, but it was of an abnormal character. When touched these parts could be obtusely distinguished, but when pricked with a pin there was no sense of pain. The other parts of the hand were normal.

On 24th January, 1896, the ulnar nerve was laid bare by an incision extending upwards from the pisiform bone about 7 centims. The tendon of the flexor carpi ulnaris was found lying un-united, having been divided at the time of the accident along with the nerve. Both the central and peripheral segments of the ulnar nerve were abnormally thick. The proximal segment of the nerve ended in a hard bulb, about the size of a small hazel nut, which was adherent to the tissue around. This bulb terminated in a tapering strand of tissue, which, however, had no apparent connexion with the distal segment of the nerve. The peripheral segment of the nerve extended upwards behind the central bulb for a short distance, and was very firmly bound down to the deeper tissues by cicatricial bands. There was no bulb upon this, but it presented a conical ending, terminating also in a strand of tissue, which had no apparent connexion with the central segment. The bulb was cut off from the central segment, and about 4 millims., including the conical ending, removed from the peripheral segment, and in both cases the exposed sections displayed the appearance of nerve tissue. The nerve was then sutured with chromic catgut, passed through the whole thickness, and, after the tendon of the flexor carpi ulnaris had been repaired, the wound was closed, no drainage being used. The arm was bandaged to a splint, with the hand fully flexed.

Three days after the operation there was distinct sense of touch on the inside of the ring finger, but none, not even the obtuse sensation present before the operation, on the little finger. Five days after the operation the patient cried out when the inside of the ring finger, or either the back or front of the little finger, was pricked with a pin, although her head was covered, and she was unaware of what was being done. On the eighth day the wound was dressed, and found healed, and it was found that the senses of touch and pain over the affected area were good, except at the tip of the little finger, where sensation was not distinct. On the twelfth day the sensation was again tested, and it was found that all parts touched with the point of a pin were correctly localised, except over the tip of the little finger. Though felt, sensation was not so distinct as in the normal hand. She cried out when pricked with a pin in any part of the affected area, except over the tip of the little finger. The stitches were removed from the cutaneous wound, and on pressure over it the abnormal sensation formerly felt had disappeared, and the flexor carpi ulnaris was felt as a tense cord. The flexion of the hand had been by this time gradually relaxed, and the arm was put on a splint, with the hand now extended. Electrical treatment was commenced, and, while the faradic current gave no response, the galvanic current gave contractions on closing, in the small muscles of the little finger, but none could be detected in those of the palm. On the twenty-eighth day the sensation was again compared in the two hands. The patient then stated that she felt touch on the inside of the palm and back of the hand, and on the inside of the ring finger, quite as well as in the corresponding parts of the left hand, but that the sense of touch on the first and second internodes of the little finger, while nearly as distinct, was not quite, while in the terminal phalanx of the little finger gentle touches with the point of a pin were felt, but very indistinctly. When pricked with a pin at any part other than the terminal phalanx of the little finger, pain was the result, but in the latter the sensation was only that of touch. By the beginning of the second month, the nutrition of the ulnar distribution of the hand was showing signs of improvement, and sensation was improved in the terminal phalanx of the little finger, pain being felt on pricking with a pin, as far as 4 millims.

from the tip. The thermic sense was tested and found correct. By six weeks from the date of operation, the last occasion upon which she was seen, the atrophy was less, though still well marked, and, while the sensation remained almost perfect, there was scarcely any improvement in motion. While she registered 22 kilos. on the dynamometer with the left hand, she could only register 4 kilos. with the right.

III.—Deductions from the Results of Operation.

Cases of secondary suture are much more valuable for the study of certain questions in the regeneration of nerves, than are cases of primary suture. In the former, if the interval of time elapsed from the time of section till the operation undertaken for repair, is sufficient to allow a condition of stable equilibrium of the parts to be attained, the deductions drawn from the results of operation are much less open to dispute. I have shown in the first part of this paper, that theories have been put forward to account for the early return of sensation after nerve suture, without admitting the restoration of conductivity of the nerve, and the question to be decided in the cases just described, is whether the return of function established, is due to a true reunion of the nerve, or if it can be explained in any other way. I would refer especially to the condition of sensation before and after operation. In the first three cases, before operation, it was carefully determined that sensation was totally lost in the regions of the skin supplied by the injured nerves, this loss including not only the sense of pain, but also that of touch. In the fourth case it was also determined that the sense of pain was absolutely lost in the region supplied by the ulnar nerve, but that there was an obtuse sense of touch present on the little and inside of the ring fingers, sufficient to enable the patient to know when her finger was touched. I take this to be the mediate sensibility, described by **Létiévant** (82), as sensation produced by the impact against the anæsthetic region, being communicated to neighbouring sound papillæ, and thus conveyed along other nerves, without any direct nerve communication existing between the part touched and the nerve conducting the impulse. Thus the impulse produced by touch might in this case have been conducted along the median or radial nerves, and learned from experience by the patient to be, from its obscure character, referred to the anæsthetic area. The absence of the sense of pain pointed to the conclusion, that the ulnar nerve was not conducting, a conclusion which was justified at the operation, as the nerve was found completely divided, and the ends lying apart. Leaving out of account the case in which the nerves were compressed at the seat of fracture, these observations were made at three, six-and-a-half, and eighteen months respectively, from the time of injury, and after the operation the sense of pain made its appearance, in one at the end of two days, in one at the end of three days, and in one at the end of five days. I have already quoted some of the published cases with similar results, and shown that none of the theories which have been advanced to account for early return of sensation by channels other than that of the injured nerve, are applicable to such as these. The finer anastomoses described by ARLOING and TRIPIER (70), or coarser anastomoses, cannot have existed in these cases, as the sense of pain was totally lost; and the delay between the division of the nerve and the operation, without any return of sensation, shows that no replacement, either by outgrowth from neighbouring nerves as supported by TILLMANNS (123), or by development of fine collateral anastomoses as held by REMAK (87), could have taken place. The speedy return of sensation after the operation, therefore, leaves only the conclusion that the return was the result of restoration of conductivity in the injured nerve. In making the tests for returning sensation, the sense of pain was always taken by means of pricking the skin with a pin, in order to avoid the possibility of mistaking mediate for immediate sensibility; for by mediate sensibility only touch is appreciated, and pricking the skin with a pin, if felt, would only be as tactile sensation.

From the time of the first appearance of the sense of pain, sensation gradually improved in the further course of the cases; but the cases showed differences in progress. At first localisation of sensation was imperfect, but this very soon was developed, and in about a month from the time of operation, in two of the cases, the gentlest touches were distinctly felt and correctly localised. In one of the cases the tip of the forefinger, and in another the tip of the little finger, were particularly long in developing sensation. In the case in which the nerves were interrupted at the seat of fracture, the return of sensation was less satisfactory, and it was not till the eighth day that the sense of pain appeared in the palm, and not till six weeks that it commenced to return in the fingers. This delay must be explained by the different nature of the lesion in this case from that in the other cases. In the latter the injury to the nerve was merely division, while in the former an indefinite length of nerve was injured by the pressure of cicatricial tissue; and although portions were removed which seemed to be most involved, doubtless there were portions at a lower level left, which were also much damaged by the pressure. The return of sensation in the ulnar distribution in the first case is particularly remarkable; for in that case the divided ends of the ulnar nerve could not be brought together nearer than about 6 millims.; and yet in the little finger the sense of pain was developed in three days. It must, therefore, be supposed either that the interval between the nerve ends was bridged over in that time by a substance capable of conducting, or that by anastomotic fibres the impulses were conducted along the median nerve in which the ends had been brought into apposition; but from the speed with which sensation in the little finger became perfected, it is more likely that the first view is correct.

In no case did improvement occur in the muscles until a comparatively late period, and as far as I was able to trace the cases, this function only approached a perfect recovery in one case (Case II), and even in that case at the end of a year it was still improving. This delay in the return of motion is an almost generally observed occurrence, and some authors, explaining away the return of sensation, take only return of motion as a proof of the restoration of the conductivity of the nerve. But the delay in the return of the motor function is easily intelligible when it is remembered that for the recovery of motion, not only the nerve, but also the muscle must undergo repair; while for sensation, only the recovery of the nerve with its end organs is necessary. The injury to the muscle is not only the result of its long inactivity, but also of its long separation from its trophic centres. Thus it is that in all the cases, even the third case, where the separation from the centres must have been less than two months, the muscles affected showed great atrophy, and tested electrically, gave the reaction of degeneration. Supposing, then, their nerve supply to be restored at the time of the first appearance of sensation, the muscles only then would begin to recover, and, in their weakened condition, their recovery must necessarily be a very slow process; and indeed, it is intelligible that in some cases the muscles would be incapable of repair from their complete degeneration. The gradual improvement in the first case was demonstrated by the return of faradic irritability in the small muscles of the thumb, one and a half months after the operation. The return of motion is also hindered by stiffness in the joints; for, in one of the cases, although at the end of a year all atrophy had disappeared, and opposition of the thumb to the tip of the little finger, and abduction of the thumb were easily performed, and although the strength of grip as tested by the hand dynamometer, was almost as good as that of the sound hand, yet the stiffness of the terminal joints of the index and middle fingers interfered with the strength of grip for smaller objects, as it was impossible to bring the tips of these fingers into the centre of the palm. (Plate 5, figs. 1 and 2.)

The operation in none of the cases gave rise to any untoward symptom. Temperature remained normal throughout, and the wounds healed by first intention. In the second case, however, after the wound had apparently healed by first intention, a small pustule formed, and pointed in the line of incision. On opening it, the sutures which had been employed for the nerve came away, and the wound then speedily healed.

The condition of the nerves found when exposed for suture was not the same in every case. In every case the nerves appeared thickened as far up and down as they were exposed, and this was not only exhibited in the central segment, but also in the peripheral. The usual description of the peripheral segment which has been some time separated from the central, is that it is found atrophied, but I did not find this in any case. On the contrary, when the nerve had been sutured, it appeared as a cord of uniform thickness above and below the seat of the suture. The divided ends of the nerves were found in one of two conditions. In two of the nerves they were united by a bulky cicatricial mass, while in two they were lying apart without any apparent connexion one with the other. Where the nerve ends were united this union was evidently not such as to enable function to be carried on. Where the ends were lying apart the central end in both cases presented a bulb of hard consistence, in one case ending in a tapering filament; while the peripheral end presented in the one case a small hard bulb, and in the other a conical ending. What may have had something to do with the different character of the two peripheral ends, is the fact that the end with the bulb was lying free in loose connective tissue, while the end with the cone was lying firmly bound down to the underlying structures by means of cicatricial bands. The prevailing opinion is that it is useless to do more than raw the peripheral end before suturing, but I always cut off the terminal portions, and the sections exposed always showed an appearance resembling the section of a nerve.

IV.—MICROSCOPICAL EXAMINATION OF THE PORTIONS REMOVED PREVIOUS TO SUTURE.

1. *Methods.*

In every case the portions removed were immediately put into **MÜLLER's** fluid, in which they remained for several weeks, the fluid being changed at intervals. After dehydration they were imbedded in paraffin, and both longitudinal and transverse sections prepared with the Cambridge microtome, the sections being cut as thin as possible. The sections were then fixed by the albumen method on slides in series, and stained by various methods. The methods which I found to give the most useful results were the first method of **WEIGERT**,* and the anilin-blue method of **STROEBE** (158). I found it useful after staining by **WEIGERT's** method to stain the preparation first with safranin and then with eosin, as by that addition the distribution of the nuclei and of the connective tissue was very clearly demonstrated.

2. *Microscopical Appearances.*

THE following Table shows the portions examined.

Part examined.	Nerve.	Case.	Time between injury and excision.
Central bulbous end	Ulnar	I.	6½ months
„ „	„	IV.	18 months
Peripheral bulbous end	„	I.	6½ months
Peripheral conical end	„	IV.	18 months
Cicatricial intercalary segment	Median	I.	6½ months
„ „ „	„	II.	3 months
Portion compressed at seat of fracture	„	III.	Uncertain
„ „ „ „	Musculo-spiral with radial and posterior interosseous	III.	Not less than four weeks

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* *Vide* LEE, 'The Microtomist's Vade-mecum,' Lond., 1893, 3rd edition, p. 362.

a. Central Ends.—The bulbs from the central segments were both very dense with smooth surfaces. One lay surrounded by loose connective tissue, while the other was adherent at its lower end to surrounding cicatricial tissue. The latter had a terminal filament, but with that exception their appearance was similar. The following are the microscopical characters of that from the ulnar of Case I. :—

Under a low power, a longitudinal section shows the nerve entering the bulb at the side. The individual fasciculi bend round in entering the bulb, and when they have entered, the fibres diverge, and spread in different directions throughout the bulb, the fasciculi presenting thus at their entrance a fan shape. The bulb itself has a clearly demarcated outline of connective tissue, but its interior presents a heterogeneous aspect. In a common ground of connective tissue, there is everywhere thickly scattered small bundles of nerve elements. These bundles are cut in all directions, some transversely, appearing as small round points, others longitudinally, appearing as lines which frequently bifurcate, and others in all degrees of obliquity. Here and there multitudes of transversely-cut bundles are grouped together in islets, surrounded by longitudinally-cut bundles.

Under a high power (Plate 7, figs. 1, 3, 5), the upper part of the entering fasciculi shows chiefly normal nerve fibres, but the lower part, while showing occasionally a normal nerve fibre, is made up of a mass of delicate bands. While the old fibres measure in diameter about 9μ, the bands measure only about 3μ in diameter. They have attached to their sides numerous nuclei, the length of which is from five to eight times their breadth, the more elongated measuring 13μ in length, and $1{\cdot}6\mu$ in breadth. These bands have a granular appearance, and there is little doubt of their being young nerve fibres, seeing that in the centre of many, a delicate thread, the axis-cylinder, can be clearly distinguished. In many also WEIGERT's method brings out a delicate myeline sheath, appearing as closely-set, bluish-black granules. In the fasciculi which enter the bulb, these new-formed fibres lie in bundles, separated by a few connective tissue fibres, running parallel with the nerve fibres. In the region of transition between the old fibres and the new (Plate 7, fig. 5), an actual connexion between the axis-cylinders of the old and those of the new cannot be traced. What, however, is clear, is that each bundle of new fibres corresponds to a single old fibre, and in many cases the old fibre can be seen tapering off, its place being taken by the new fibres, the number of new fibres becoming greater as the old fibre diminishes, until finally only new fibres remain. In tracing further downwards the groups of new fibres, the number contained in a single bundle increases, and, while the bundle is thereby increased in diameter, the fibres themselves retain a fairly uniform breadth.

Passing into the bulb, there are here no old fibres to be found, but the whole structure is made up of bundles of new fibres, cut in every direction, and surrounded by a small amount of fibrous tissue. The bundles cut transversely are small in diameter (Plate 7, figs. 1 and 3), yet the larger contain an enormous number of young nerve fibres. These fibres appear as clearly defined circles, containing each in its centre a distinct axis-cylinder. The more prominent have a diameter of 3μ, but there are some which have not more than half that diameter. Many have attached to their sides a nucleus, which here has a circular outline, but which, when compared with those in a longitudinally-cut bundle, is seen to be a section of a spindle-shaped nucleus. The whole bundle is surrounded by a layer of connective tissue, but there is no sheath proper. The fibres which show longitudinally, present the same characters as the new fibres in the entering nerve already described.

Transverse sections of the upper part of the entering nerve in the central bulb of Case IV., show that at this point the nerve has retained its normal arrangement of fasciculi. While some of these fasciculi have retained at this level their normal fibres, others have no old fibres, but instead, groups of young fibres (Plate 8, fig. 1). These young fibres present characters identical with those of the fibres in the bulb already described, but, as a rule, only from three or four up to a dozen are grouped together in a single bundle. These bundles resemble very closely, both in number and in disposition, the arrangement of the single old fibres in neighbouring fasciculi in which the latter have been retained. Around these fasciculi the perineurium and epineurium present normal characters, and the endoneurium appears also to be normal.

The examination of the filament in which the bulb terminated, was made by serial transverse sections. It is composed almost entirely of connective tissue, but at its upper end there are about twenty or thirty small bundles of new nerve fibres. Proportionately as the sections are taken from lower levels, the number of nerve fibres diminishes, and the last section examined, still some distance from the termination of the filament, contains only three small bundles, each containing three or four young nerve fibres.

b. Peripheral Ends.—The bulbous end, removed from the peripheral segment of the ulnar in Case I., was about half the size of that removed from the central end, and had also a firm consistence.

Under a low power, it presents a ground-work of connective tissue, in which lies tissue stained bluish-black by WEIGERT'S method. This tissue runs in bundles, longitudinally from the point at which the bulb was removed, towards the free end. About the middle of the bulb, the more regular longitudinal course of these dark stained bundles ceases, and the remainder of the section is occupied by the same tissue, cut transversely and in various degrees of obliquity, showing thus many circular bundles, isolated or in groups, with a few bundles running longitudinally for a short distance among them.

Examined with a high power, the sections show no old nerve fibres, but the tissue stained by WEIGERT'S method is identical in characters with the new nerve tissue seen in the central bulb. In the distal half of the bulb, the fibres run chiefly longitudinally, and are grouped into bundles, each of which contains many nerve fibres. These young fibres have the same characters as those in the central bulb. Thus they have the same average diameter, have attached to their sides at very short intervals, elongated nuclei, and have in many cases a delicate myeline sheath. In many, a distinct axis-cylinder is visible, occupying the centre of the fibre. The bundles are separated by fibrous tissue in greater or smaller amount, and in this tissue are a number of round cells with granular contents. A few bundles appear cut transversely, beside those cut longitudinally. In the proximal half of the bulb it is rare to get the fibres running for any great distance in one plane. Thus the majority appear cut transversely or obliquely. The connective tissue here is in larger quantity than at the attached end of the bulb. The bundles of nerve fibres cut transversely are of different size, but, irrespectively of that difference, the contents are identical. They contain (Plate 7, figs. 2 and 4) from a few up to twenty or thirty closely aggregated young nerve fibres. The larger of these measure in diameter 3μ, have a well-defined circular outline, and contain each in its centre a distinct point, the axis-cylinder. There are also many much smaller fibres with similar characters. The bundles also contain the sections of nuclei, the larger of which are about one half the diameter of the larger fibres. Around the bundles, one or two layers of connective tissue are arranged concentrically, but there is no definite sheath.

The conical portion removed from the peripheral segment in Case IV., also contains no old nerve fibres. It has a very dense structure, the nerve elements and connective tissue being very closely aggregated together. A few transverse sections removed from the base of the cone, show the majority of the new fibres in bundles cut transversely (Plate 8, fig. 2), but even at that level a few are cut longitudinally and obliquely. Similarly, in longitudinal sections of the cone, there is no part in which the bundles run exclusively in one direction. Towards the apex of the cone the number of fibres diminishes, and the section appears entirely composed, ultimately, of connective tissue. The characters of the fibres here are identical with those of the fibres already described, but a few show the formation of the myeline sheath more distinctly than those either in the peripheral or central bulbs of Case I. In some of the fibres, it has taken on the stain so deeply that the contents of the fibre are quite hidden, and it appears as a uniform granular coat.

The cone terminated in a filament about 12 millims. in length, and this was examined for nerve fibres by serial transverse sections, but none were found. The core of the filament is occupied by a blood vessel, and the remainder is simply connective tissue.

c. *Intercalary Cicatricial Segments.*—The cicatricial mass which united the two ends of the median in Case I., measured 1·5 centim. in length and 1 centim. in breadth. It had a rough and somewhat irregular surface and firm consistence. It was thicker in the middle, and narrowed to the thickness of the nerve at either end.

Transverse sections from its proximal end (Plate 8, fig. 3) show a network of dense fibrous tissue, containing in its meshes bundles of nerve elements. In some parts the connective tissue fibres run longitudinally, appearing as points in section, but in others they run transversely, being there displayed in a large part of their course in the section. The bundles of nerve elements are uniformly distributed throughout the section, but they are small, the larger measuring only 30μ in diameter, and are isolated from each other by a considerable breadth of dense fibrous tissue. Some are very small, containing only two or three fibres, while the larger contain as many as twenty. All the fibres exposed are small new fibres, no old fibres being present. These fibres agree in characters with those already described. They have a very sharply defined outline, the axis-cylinder is very distinct, and there are many nuclei lying between them and attached to their sides. Many of these fibres are larger than any met with in the other cases, some measuring 4μ in diameter.

The distal end of the mass presents a less regular aspect. In some parts (Plate 8, fig. 4) there are dense masses of fibrous tissue, and only isolated bundles of nerve elements, grouped together, while in other parts (Plate 9, fig. 1), the distribution of the nerve elements is very uniform. These uniformly distributed bundles are still smaller than the bundles in the proximal end, the largest measuring 17μ in diameter, but the majority much smaller. The larger contain eight or ten young fibres, and the smaller from two to three or four. In addition to these, there are many isolated fibres. The young fibres are the same in structure as those in the opposite end of the mass. The bundles do not all appear in transverse section, but a few appear running longitudinally in the section, and, therefore, transversely in the mass, and a few obliquely cut. In these the spindle-shaped nuclei attached to the sides of the fibres are displayed. Also in many such fibres the axis-cylinders are shown as delicate threads (Plate 8, fig. 4).

The characters of this mass, which have been described from transverse sections from its two opposite ends, are shown by longitudinal sections to be maintained throughout the whole mass. The arrangement of the bundles is very irregular. In the same longitudinal section are to be seen islets of transversely-cut bundles (Plate 8, fig. 5), and coursing around them, bundles cut longitudinally and obliquely. Some of the longitudinally-cut bundles contain fibres which show very well the developing myeline sheath, not, however, sufficiently dense to hide the delicate axis-cylinder (Plate 8, fig. 6).

The intercalary mass from the median of Case III. agrees in characters with that just described so closely that a separate description is unnecessary.

d. Portions Compressed at Seat of Fracture.—The portion excised from the median, and that from the musculo-spiral with its two branches, are examples of nerves which have been under compression for several weeks.

The portion excised from the median measured in length only about 12 millims., yet transverse sections from the proximal and distal ends show very different structures. The transverse section of the proximal end (Plate 9, fig. 2) is practically that of a normal nerve, showing throughout a normal subdivision into fasciculi, surrounded each by a normal perineurium, and each containing normal myeline fibres, the majority of which measure about 8μ in diameter. The section agrees in every particular with transverse sections of normal human nerves, which were treated by the same methods for comparison. The transverse section of the distal end shows a normal subdivision into fasciculi, and, under a very low power, looks like the section of a normal nerve, with the exception that, treated by WEIGERT'S method, the fasciculi are not stained so deeply. With a high power, however (Plate 9, fig. 3), the difference from the normal nerve is very decided, for the fasciculi contain no old myeline fibres, but in their place groups of young fibres. The perineurium surrounding each of the fasciculi has a normal appearance, but the endoneurial tissue has, if anything, a stronger development than normally. The groups of young fibres are small, the majority measuring about 8μ in diameter, with here and there a few larger examples. As a rule, they contain only three or four young nerve fibres, each presenting a sharp circular outline, and containing an axis-cylinder in its centre, together with one or two nuclei, either lying between the young fibres or at the circumference of the small bundle. Most of the bundles are surrounded by a delicate membrane. All the bundles shown in the section are transversely cut. The epineurium is normal, and no young fibres are found between the layers of the perineurium.

The portion removed from the musculo-spiral nerve and its two branches included the terminal 12 millims. of the former, with 6 millims. of the radial, and 3 millims. of the posterior interosseous. The transverse section of the proximal end of the musculo-spiral is normal, while those of the distal ends of the radial and posterior-interosseous present no old nerve fibres, but instead, groups of young fibres arranged as in the distal end of the portion of the median just described. In the transverse sections which have passed through the region of transition from the old fibres to the new, some of the fasciculi show an arrangement of old myeline fibres which is that of a normal nerve, but many of the myeline fibres have an abnormal character. In the simplest of these, the axis-cylinder is greatly hypertrophied, and the whole fibre is enlarged (Plate 9, fig. 5). In others, between the sheath of SCHWANN and the myeline sheath is a large nucleus, presenting a circular outline. In another, in addition to the large nucleus, and lying alongside of it, are one or two very distinct young nerve fibres with clearly-defined circular outlines, and delicate axis-cylinders, while the myeline sheath of the old fibre is indented by the new-formed structures, and the old sheath of SCHWANN is slightly distended (Plate 9, fig. 5). The old fibre, however, has still its characters preserved. The majority of such old fibres measure about 12μ in diameter, while the new fibres intercalated between the sheath of SCHWANN and the myeline sheath measure 3μ in diameter, and the nucleus has a diameter approximately the same. Other old fibres in the same section present three, four, and up to a dozen newly-formed fibres lying in the same position, and the number of nuclei present is proportionately increased to two, three, or more. Just as the old fibres present a greater number of young fibres, so the old myeline sheath and axis-cylinder appear crushed to the one side and diminished (Plate 9, figs. 6 and 7). In some, in which the old sheaths of SCHWANN contain about a dozen new fibres, traces of the old axis-cylinder and myeline sheath can still be seen at one side of the group, while, in other cases, no trace of the old myeline sheath and axis-cylinder can be found, and there is merely a group of young fibres with nuclei, surrounded by the old sheath of SCHWANN. Those old fibres, which still contain the myeline sheath and axis-cylinder, and yet have young fibres between the myeline sheath and sheath of SCHWANN, show the latter sheath distended in proportion to the number of young fibres present. Also, where the myeline sheath and axis-cylinder of the old fibres have disappeared, many show the old sheath of SCHWANN surrounding the group of young fibres, but, in some, where the number of young fibres in a bundle is great, the old sheath of SCHWANN is very difficult to trace.

A longitudinal section made through the same region shows the old myeline fibres terminating and giving place to the young fibres (Plate 9, fig. 4); and the sheath, enclosing the bundle of young fibres, can often be traced into continuity with the old sheath of SCHWANN. The more common condition traced from the old fibre above down into the bundle of young fibres is as follows:—The old fibre gradually increases in diameter, and presents finally what approaches a bulbous condition. In its interior the axis-cylinder is swollen and presents in many cases a bulb. Beyond this the old myeline sheath and axis-cylinder contract greatly and terminate almost immediately. The sheath of SCHWANN is continued beyond the bulbous myeline fibre as the sheath surrounding the bundle of young fibres. Often, before the termination of the old fibre is reached, isolated young fibres can be seen, running between the sheath of SCHWANN and the myeline sheath. These pass downwards, until they are lost in the bundle of young fibres beyond the old. The nuclei seen in transverse sections as circular are here shown to be spindle-shaped.

V.—DEDUCTIONS FROM THE MICROSCOPICAL APPEARANCES.

1. *Degeneration.*

The length of time which has elapsed from the time of injury till the examination of the nerve in these cases, precludes the study of the earlier stages of degeneration, but allows certain deductions concerning the later stages and final result of the process.

The sheath of SCHWANN, notwithstanding the lapse of several weeks from the commencement of compression, still remains in the portions of nerve from Case III. (Plate 9, fig. 3). It can be traced downwards from the old fibre into the region of the new fibres, where, for a time, it is retained (Plate 9, fig. 4). But as the new fibres increase in numbers, the old sheath is gradually distended, and ultimately becomes unrecognisable, probably becoming part of the endoneurial connective tissue. This, then, accords with the view expressed in the recent papers by **Büngner** (150), **Howell** and **Huber** (156), **Stroebe** (158), and **Notthafft** (159), that the sheath of **Schwann** is retained for a time after degeneration of the other parts of the fibre, but that it is destroyed during the regenerative process.

Where the old sheath of **Schwann** is still retained, it contains nothing which could be taken for the old axis-cylinder. The latter, traced into the region of compression, is seen terminating, often in bulbous ends, and below that, the contents of the old sheath are only new-formed elements (Plate 7, fig. 5; Plate 9, fig. 4). In other cases, the gradual disappearance of the old axis-cylinder can be seen in transverse sections through the point of transition from old to new fibres (Plate 9, figs. 5, 6, and 7). In the portions of nerve removed from peripheral segments there are no old fibres to be seen, and no structures which could be taken for old axis-cylinders. My results are, therefore, not in accord with the view taken by **Schiff** (31), **Philipeaux** and **Vulpian** (39), **Wolberg** (127), and others, that both the old sheath of **Schwann** and the old axis-cylinder are retained in the whole peripheral segment. **Ranvier** (102), also, while he finds that the axis-cylinder is destroyed in the peripheral segment, holds that it is retained in the central, unless exceptionally, and that the degenerative process affects only the extremely small portion of the central segment measured by one or two of the nodes now called by his name. But in the central bulbs examined there are portions of the old nerve, about 6 millims. in length, attached to the side of the bulb, and it is only at the extreme upper part of this that old fibres are present, while the remainder is entirely occupied by new fibres, among which no trace of the old axis-cylinders is visible.

The view taken by **Krause** (136) that the sensory fibres from the touch corpuscles of **Wagner** and **Meissner**, having their nutritive centres there, undergo degeneration in the central segment, while they remain sound in the peripheral segment, has been taken as an explanation of the conflicting results of other authors. **Krause** found that transverse sections of the central segment showed about one-half of the fibres degenerated, while he merely assumed that in the peripheral segment there were a corresponding proportion of the fibres which remained sound, his assumption being based on analogy with the condition found in rabbits. But in the transverse sections made from the proximal ends of the portions from the median and musculo-spiral nerves of Case III., the appearances presented are those of a normal nerve (Plate 9, fig. 2); in none of the fasciculi are any new fibres found, and there has therefore been no degeneration. Also, in portions removed from peripheral segments, no old fibres are present. I cannot, therefore, agree with **Krause** that there is an immediate ascending degeneration in the central segment, for the proportion of fibres indicated by him as becoming degenerated in the central segment is so great that there would be no difficulty in seeing them if present, or the resulting regeneration in any case. This is also the opinion expressed by **GOTTSACKER** (145) from examination of stump neuromata. From the account given by S. **MEYER** (100, 108, 125), **HAMMER** (161), and **TEUSCHER** (149), it would appear that in any nerve there are always to be found degenerated fibres; but that these are present only very sparingly, and are due to a normal process of degeneration. **KRAUSE'S** results were obtained from the examination of nerves in limbs amputated for gangrene. Several of these were senile or diabetic gangrene, and it is, therefore, possible that in his cases the degeneration of the nerve was primary to the gangrene. This is more likely, if we are to regard, with S. **MEYER**, the nerve fibres, not as perennial structures, but as undergoing a normal process of degeneration and regeneration; and this view is supported by the work of **KORYBUTT-DASZKIEWICZ** (105), who found an active formation of nerve-fibres in the nerves of the frog, on placing the frogs in favourable surroundings, after a period of starvation. In any case, if an immediate ascending degeneration were caused by interruption of the course of a nerve, there would have been some evidence of that in the transverse sections of the proximal ends of the median and musculo-spiral portions from Case III.

2. *Regeneration of nerve fibres in the peripheral segment, while still separated from the central segment.*

The portions of nerves examined show very clearly, not only that in regeneration the young fibres are produced both in the central and in the peripheral segment, but also that reunion of the ends is not an essential to the production of young fibres in the peripheral segment (Plate 7, figs. 2 and 4; Plate 8, fig. 2). This independent origin of new fibres in the peripheral segment, without previous reunion with the central end, first observed and described by **PHILIPEAUX** and **VULPIAN** (38, 39), has been opposed by almost all who have since made a study of regeneration of nerves; and their opinion was also greatly weakened by the fact that **VULPIAN** (77, 86) himself withdrew from his former position. **MITCHELL** (80), and recently **BOWLBY** (146) have found in the examination of portions removed from the peripheral segments of un-united divided nerves, that many newly formed nerve fibres are there present. The opponents of this view give various explanations of the results of these observers. Some hold that **PHILIPEAUX** and **VULPIAN** mistook products of degeneration for young fibres; **SCHIFF** (41), and **AMBROSOLI** (43) that their results were only to be got in very young animals; while **RANVIER** (102), again, thinks that they did observe the peripheral segment regenerated, but that they had failed to observe certain strands of tissue between the central and peripheral ends, through which the peripheral segment had been regenerated. He supports this allegation by an observation of his own, where a central segment lying separate from its peripheral, was connected to it by a membrane having the appearance of connective tissue, but which contained nerve fibres, as shown by the tint which it took on being subjected to the action of osmic acid. **Howell** and **Huber** (156) in opposing the results of **Bowlby**, hold that the young fibres which he observed, were simply sections of nuclei, and that the point in their interior, taken for the axis-cylinder, was nothing more than the nucleolus, and state that this explanation is more likely, since **Bowlby** figures no nuclei among the bundles of fibres. It is true that in **Bowlby**'s figures there are no nuclei shown among the young fibres, and he believes that the axis-cylinders are formed by the nuclei. But in my preparations there can be no doubt of the structures in question being young nerve fibres ; for the axis-cylinder shown in transverse section as a point, is clearly visible in many fibres seen longitudinally, as a delicate thread. Also in the bundles which are cut transversely, nuclei are always present (Plate 7, fig. 4), lying between the fibres, and in many cases distinctly attached to the fibres ; and in fibres seen longitudinally these nuclei are spindle-shaped, and distinctly attached to the sides of the fibres. The difference between the axis-cylinders and the nuclei of a bundle is well shown in some of the preparations, which were stained by the method recommended by **Stroebe** ; for the former have taken on the aniline blue, while the latter have taken the red colour of the safranin. But that they are really nerve fibres, does not rest alone on the axis-cylinder being demonstrated, for they also in many cases show a commencing myeline sheath. In order to find if they could possibly have been communicated to the peripheral segment from the central end of the nerve through fine bands of tissue connecting the ends as suggested by **Ranvier**, I made a careful search for such. In one of the cases such were present, in the form of fine filaments, one attached to the central end, and one to the peripheral, but without any connexion one with the other. In that attached to the peripheral, there were no nerve elements present, while in that taken from the central end, the upper portion contained only a few isolated bundles of young nerve fibres, which gradually diminished in numbers, as the sections were taken further away from the bulb, until in the last section taken, still some distance from the termination of the filament, only three small bundles remained. I found, therefore, no means of communication between the ends, and must conclude that the young fibres observed in the peripheral segment have an independent origin there.

Vanlair (122) found in the sciatic nerve of a dog, that four months after resection of a portion there was reunion of the ends by a cicatricial segment, but no functional return. The cicatricial segment, he found regenerated, but the peripheral segment contained only fibres which he regarded as end products of degeneration, and called "atrophic degeneration." His description of these fibres agrees with the appearance presented by newly-formed fibres, and I think it probable that they were such, and not the products of degeneration.

3. *The Origin of the Young Fibres.*

The arrangement, wherever they are found, of the new fibres in bundles suggests that the fibres composing each bundle have had a common origin. As a rule, the number contained in a single bundle is great. The part of the nerve in which they originate can be seen, when sections from the central segment close to the termination of the old fibres are examined; for, while the young fibres are there seen still in bundles, these bundles are small, and contain few young fibres. The diameter of these small groups of fibres is approximately the same as that of a single old fibre, and the sheath of SCHWANN can be traced down in longitudinal sections, from the old fibre into the region of the new, where it is seen surrounding the small bundle of new fibres (Plate 9, figs. 3 and 4). It is clear from this that these young fibres originate within the sheath of SCHWANN. On tracing them downwards in longitudinal sections, they are found to increase in numbers and distend the sheath of SCHWANN, which ultimately becomes unrecognisable. It is thus probable that the young fibres of each of the bundles which appear in the central bulb and in the end of the peripheral segment, represent in most cases fibres which have had a common origin from within one old sheath of SCHWANN.

The epineurium and perineurium appear normal in the portion of nerve immediately proximal to the central bulb, and in the portions removed from the seat of compression (Plate 8, fig. 1; Plate 9, fig. 3). There is, therefore, nothing to indicate an origin of nerve fibres from the cells of the perineurium as described by HJELT (44), WOLBERG (127), and HANKEN (143). Also the view of VANLAIR (122) that the new fibres proceed into the perineurium, and out into the epineurium, forming a zone round the fasciculus, has nothing to support it in my preparations.

If, then, the new fibres originate within the old sheath of SCHWANN, they must be formed either by growth from the old fibre above, as described by RANVIER (81, 102) and others; or from the remains of the old fibre, as held by many; or from the protoplasm and nuclei of the sheath of SCHWANN, as held by BÜNGNER (150) and others. The manner in which the old fibre ceases abruptly, and gives place to many young fibres which occupy the continuation of its sheath of SCHWANN, may suggest an origin such as described by RANVIER and others; but the presence of undoubted young nerve fibres in the peripheral segment, while it has no connexion with the central segment, is incompatible with this view. The young fibres also cannot originate from the remains of the old, as in the region of transition from the old to the new, both old fibres and young are seen enclosed within a common sheath of SCHWANN (Plate 9, figs. 5, 6 and 7). Thus the only source left from which to derive the young fibres within the old sheath of SCHWANN, is the nucleus and protoplasm of the interannular segment. This conclusion is strengthened by the examination of transverse sections, passing through the point of transition from the old fibres to the new; for there, the old fibre can be seen with one or more young fibres lying beside the nucleus, and between the sheath of SCHWANN and the myeline sheath (Plate 9, figs. 5 to 7). The enormous number of spindle-shaped nuclei among the nerve fibres, indicates that these structures have originated by proliferation from the nuclei of the sheath of SCHWANN, but in my preparations the proliferative stage had evidently come to a conclusion, as no indications of karyomitosis were present.

My results are, therefore, in accord with the opinion expressed in **Büngner's** recent paper, that the nuclei and protoplasm of the interannular segments must be viewed as neuroblasts, their function being to produce new nerve fibres. And, taking into account the observations of S. **Meyer** (100, 108, 125), it would appear that the exercise of their function is not reserved for accidents such as nerve section, but occurs normally, the fibres undergoing a normal degeneration and regeneration. The bundles of young fibres were seen by **Howell** and **Huber** (156) in the peripheral end of nerves which had not united, but having failed to stain the axis-cylinder they call them "embryonic fibres," and find that they receive axis-cylinders only by growth of the latter from those of the old fibres in the central end. That these fibres observed by **Howell** and **Huber** were really nerve fibres, is shown by the fact that when the peripheral segment, containing only such, was mechanically irritated, a low degree of irritability and conductivity was found.

4. *Characters of the Young Fibres.*

The young fibres appear with a central axis-cylinder, with a protoplasmic surrounding zone, having a well-defined outline, and with spindle-shaped nuclei attached at short intervals to their sides. It is evident, therefore, that the nuclei do not form the axis-cylinder as described by **Bowlby** (146), but that in the formation of the fibre only the central portion of the primitive protoplasmic thread becomes developed into the axis-cylinder. In many fibres, both in the central and peripheral ends, the protoplasmic zone contains a granular deposit which takes on the characteristic tint of myeline by treatment with **Weigert's** method (Plate 8, fig. 6). It is, therefore, clear that the myeline sheath is deposited in the protoplasm gradually and uniformly. In transverse section the young fibres correspond in appearance and in diameter (3μ) with the "fibres à gaîne vitreuse" of **Vanlair** (122), and according to him the "gaîne vitreuse" is a provisional covering of the axis-cylinder, derived from the connective tissue around, which becomes thinner as the normal sheaths of the axis-cylinder develop, and finally becomes the fibrillar sheath. I think it more probable that the zone surrounding the axis-cylinder is the protoplasmic residue not used up in the formation of that structure, and that after the myeline sheath becomes deposited within it, it remains with the nucleus as the protoplasm of the interannular segment.

Independently of the time which has elapsed from the injury till the excision of the portions of nerve examined, the stage of development of the young fibres is the same, with the exception that some show more distinctly than others the commencing myeline sheath; and this similarity occurs both in the central and peripheral ends. As this time varied from a few weeks to eighteen months, the development presented by the fibres must be regarded as a resting stage. It is probable that the further steps in development to the adult fibre depend on a restoration of continuity of the nerve, and that such as would allow the transmission of impulses through the young fibres. Also the observation of PHILIPEAUX and VULPIAN (39) that regeneration is more rapid when union is effected, may be explained on the view that reunion is necessary to the further development of the fibres. That these young fibres are capable of transmitting impulses, I take the observations of HOWELL and HUBER as proving; and this explains also why, after the operation of suture, so rapid a return of sensation in the parts previously anæsthetic occurs.

With regard to the formation of the new sheath of SCHWANN, it might be viewed as a metamorphosed outer layer of the young fibre, but this is unlikely from the behaviour of the old sheath. For, since that structure does not degenerate along with the rest of the fibre, and is only finally destroyed or displaced by the mechanical condition that it is no longer able to contain the developing fibres, it does not act as part of the fibre. It is more probable that it is an addition to the fibre from the surrounding connective tissue.

On comparing the transverse section of a nerve made through a part which contains the old fibres, with one made further down in the region containing new fibres, the increase in numbers of the new fibres as compared with the old is very striking. It is seen that the number of groups of the new fibres is approximately equal to the number of old fibres, and as each group contains at a high level three or four, and at a lower many more, the numerical increase may be roughly estimated (Plate 9, figs. 2 and 3). It is hardly likely that all such fibres are developed to the stage of maturity. It may be that when reunion is established, only the normal number of fibres develop further, while the others perish or remain undeveloped; but this is a subject upon which there is as yet no evidence.

5. *Cicatricial Intercalary Segments.*

The nature of the cicatricial mass, uniting two ends of a nerve by a bond which does not allow re-establishment of function, is illustrated by two of the cases. In these, although the mass has the appearance of cicatricial connective tissue, yet the microscopical examination shows that from end to end the mass contains a rich supply of young nerve fibres. But at the same time, these young fibres are separated by much dense connective tissue, which in some places is massed together to the exclusion of young nerve fibres (Plate 5, figs. 3 to 6; Plate 6, fig. 1). This mass has evidently been supplied with nerve fibres by immigration into it of neuroblasts, either from the central end or from both. I think from both ends, from the fact that both central and peripheral ends of nerves, remaining entirely separated, show at their ends a mass of connective tissue containing nerve fibres. The latter do not run in parallel lines, as they do when met in a piece of old nerve, but are convoluted, showing that they have been developed in the irregular spaces of the connective tissue. But if a cicatricial mass connecting the two ends of a divided nerve is thus supplied with nerve fibres from the central and peripheral ends, there must be some cause preventing the transmission of impulses. The explanation which seems to me most probable, is that if there has been much inflammation in the parts, the amount of cicatricial tissue in the mass is so great, that by the time the mass is bridged over by nerve fibres, the contraction of the cicatricial tissue has become so great, that the nerve fibres are prevented from transmitting impulses or developing further, in a way exactly analogous to that which occurs when a nerve is involved in the callus of a fracture.

VI.—General Conclusions.

1st. Un-united divided nerves, sutured long after division, can re-unite and transmit impulses in a few days.

2nd. After division or interruption of a nerve, there is no ascending degeneration of the kind described by Krause.

3rd. The old axis-cylinder is destroyed in the peripheral segment, and in the ultimate portion of the central segment.

4th. New fibres originate in the peripheral segment as well as in the central end.

5th. The formation of new fibres in the peripheral segment occurs, although there is no connection with the central end, but maturation of the fibre is not completed while separation of the ends lasts.

6th. The new fibres originate from cells within the sheath of Schwann.

7th. In the development of the young fibres, the central portion of the primitive protoplasmic thread forms an axis-cylinder, and the myeline sheath is deposited in the surrounding protoplasmic zone, which latter remains along with the nucleus as the neuroblastic element of the interannular segment.

8th. The cicatricial mass uniting the ends of a divided nerve may be permeated by young nerve fibres from end to end without functional union being effected, if the amount of cicatricial connective tissue present in the mass is sufficient by its pressure to prevent the passage of impulses.

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Explanation of Plates 4–9.

PLATE 4.

Fig. 1. Hands of Case I., before operation. Suture of median and ulnar nerves six-and-a-half months after division. Sound hand for comparison. Shows difference in quality of skin, loss of flexures, atrophy, sore on inner side of first internode of little finger, transverse depressed lines on nails, and the characteristic attitude. $\frac{1}{2}$ nat. size.

Fig. 2. Hand of Case I., before operation. Lateral view. Shows position in which the hand was carried at the wrist, lines on nail of thumb, atrophy of thenar eminence, and part of the cutaneous cicatrix from wound in forearm. $\frac{1}{2}$ nat. size.

PLATE 5.

Fig. 1. Hand of Case II., with left hand for comparison, one year after operation of suture of the median three months after division. Shows restored thenar eminence and extent to which hand can be opened. $\frac{2}{7}$ nat. size.

Fig. 2. Same. Shows extent to which hand can be closed. The inability to bring the tips of the index and middle fingers by complete flexion of their terminal phalanges into the centre of the palm is displayed. Operation cicatrix shown in middle line above wrist. $\frac{2}{7}$ nat. size.

Fig. 3. Hand of Case IV., before operation. Section of ulnar nerve of eighteen months' standing. Shows over-extension of the first phalanges and flexion of the second and third phalanges of the little and ring fingers, and the atrophy of the hypothenar eminence. The transverse cicatrix of wound above wrist is shown. $\frac{1}{2}$ nat. size.

PLATE 6.

Fig. 1. Hand of Case III., with right hand for comparison, before operation. Two months after fracture at elbow joint. Shows position in which fingers and thumb were carried, and the atrophy of the thenar and hypothenar eminences. $\frac{1}{2}$ nat. size.

Fig. 2. Same. Shows hollowing out of palm and flexion at wrist. $\frac{3}{8}$ nat. size.

PLATE 7.

Fig. 1. Longitudinal section central bulb, ulnar nerve. Case I. Near centre three small bundles grouped together, and separated by layers of connective

tissue, and each containing an enormous number of young nerve fibres, in which are displayed the axis-cylinders, each surrounded by a clear zone. A bundle also shown longitudinally, the fibres showing in parts the delicate axis-cylinder with granular deposit of myeline around, and also oval nuclei. Zeiss, Obj. D. $\frac{340}{1}$. *Cf.* figs. 2 and 3.

Fig. 2. Longitudinal section bulb from peripheral end of ulnar. Case I. Shows young nerve fibres identical in appearance with those in central bulb (fig. 1). Many nerve fibres in each bundle. Distinct axis-cylinders. The nuclei in the bundles are distinct from the nerve fibres. Zeiss, Obj. D. $\frac{340}{1}$. *Cf.* fig. 4.

Fig. 3. Same as in fig. 1. (Central end.) Part of largest bundle taking an oblique course. Zeiss, Obj. F. $\frac{600}{1}$.

Fig. 4. Same as in fig. 2. (Peripheral end.) Shows young nerve fibres with axis-cylinders and clear surrounding zone, and many nuclei interspersed among fibres. Zeiss, Obj. F. $\frac{600}{1}$.

Fig. 5. Longitudinal section ulnar nerve at entrance to central bulb. Case I. Transition from old to young nerve fibres. Shows old fibre diminishing and giving place to young nerve fibres with spindle-shaped nuclei. At one side a bundle of young nerve fibres less than double the diameter of an old fibre, showing young nerve fibres with axis-cylinders, granular myeline deposit, and spindle-shaped nuclei, attached to sides of young fibres. Zeiss, Obj. F. $\frac{600}{1}$.

PLATE 8.

Fig. 1. Transverse section of ulnar nerve eighteen months divided, immediately proximal to the bulb on central end. Case IV. Portion of fasciculus. Shows normal perineurium and small bundles of young nerve fibres arranged like single old fibres. In some a delicate sheath surrounding the bundle. Zeiss, Obj. D. $\frac{340}{1}$.

Fig. 2. Transverse section, base of cone from peripheral end of ulnar, eighteen months divided. Case IV. Shows compact tissue with small bundles of young nerve fibres cut transversely. Nuclei in the bundles besides nerve fibres. Zeiss, Obj. D. $\frac{340}{1}$.

Fig. 3. Transverse section, proximal end of intercalary segment uniting ends of median. Case I. Dense groundwork of fibrous tissue containing in its meshes bundles of young nerve fibres showing nuclei. Zeiss, Obj. D. $\frac{340}{1}$.

Fig. 4. Transverse section, distal end of same intercalary segment. Dense masses of fibrous tissue with a few bundles of transversely-cut young nerve fibres, and one bundle of young nerve fibres longitudinally cut. Zeiss, Obj. D. $\frac{340}{1}$.

Fig. 5. Longitudinal (radial) section same intercalary segment. A portion at centre of mass. Shows several bundles of young nerve fibres transversely cut. Zeiss, Obj. F. $\frac{600}{1}$.

Fig. 6. Another portion same section. Also at centre of mass. A bundle of young nerve fibres seen longitudinally. Shows axis-cylinders and commencing myeline deposit. Zeiss, Obj. F. $\frac{600}{1}$.

PLATE 9.

Fig. 1. Transverse section, intercalary segment—distal end. Another part of same section shown in Plate 8, fig. 4. Shows numerous very small bundles of young nerve fibres. Zeiss, Obj. D. $\frac{340}{1}$.

Fig. 2. Transverse section, proximal end of portion excised from median nerve. Case III. Nerve compressed at seat of fracture. Shows old myeline nerve fibres. Same appearance as section of normal nerve treated by same methods. Zeiss, Obj. D. $\frac{340}{1}$.

Fig. 3. Transverse section, distal end of same portion of nerve. Shows normal perineurium, and small bundles of young nerve fibres, grouped as the single old fibres in fig. 2. Many of the bundles contain also nuclei and are surrounded by a delicate sheath. Zeiss, Obj. D. $\frac{340}{1}$.

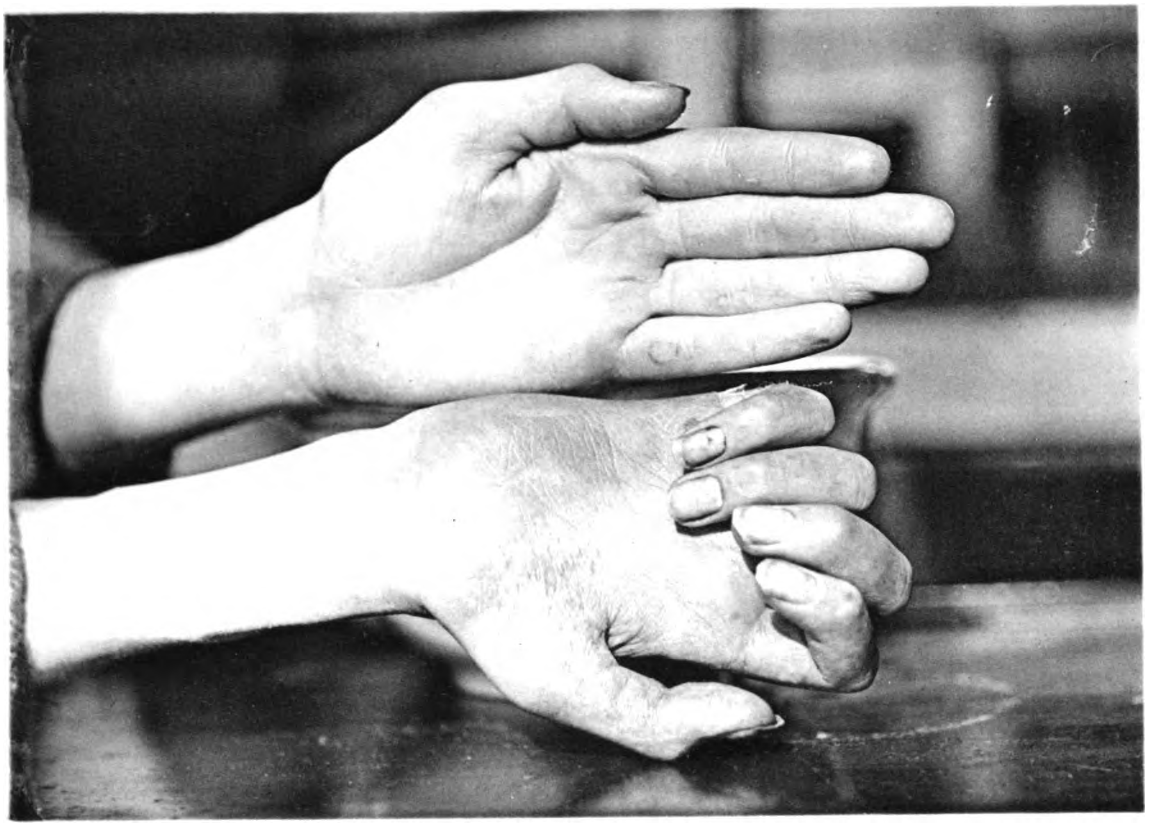
Fig. 4. Longitudinal section through point of transition from old to young nerve fibres in portion removed from musculo-spiral nerve. Case III. Two old fibres are seen terminating and giving place each to a bundle of young nerve fibres. Zeiss, Obj. F. $\frac{600}{1}$.

Fig. 5. Transverse section same. Near centre, two very large old fibres, one of which shows at one side a slight thickening representing the nucleus and protoplasm of the sheath of Schwann, while the other shows at one side a large circular nucleus with two young nerve fibres at its side, all three structures lying between the myeline sheath and sheath of Schwann. Zeiss, Obj. F. $\frac{600}{1}$.

Fig. 6. Same section. Portion of perineurium, and near centre, a bundle of young nerve fibres with two nuclei and the old myeline sheath and axis-cylinder at one side. Zeiss, Obj. F. $\frac{600}{1}$.

Fig. 7. Same section. Near centre a bundle of young nerve fibres, with remains of old fibre at one side. Zeiss, Obj. F. $\frac{600}{1}$.

Fig. 1.



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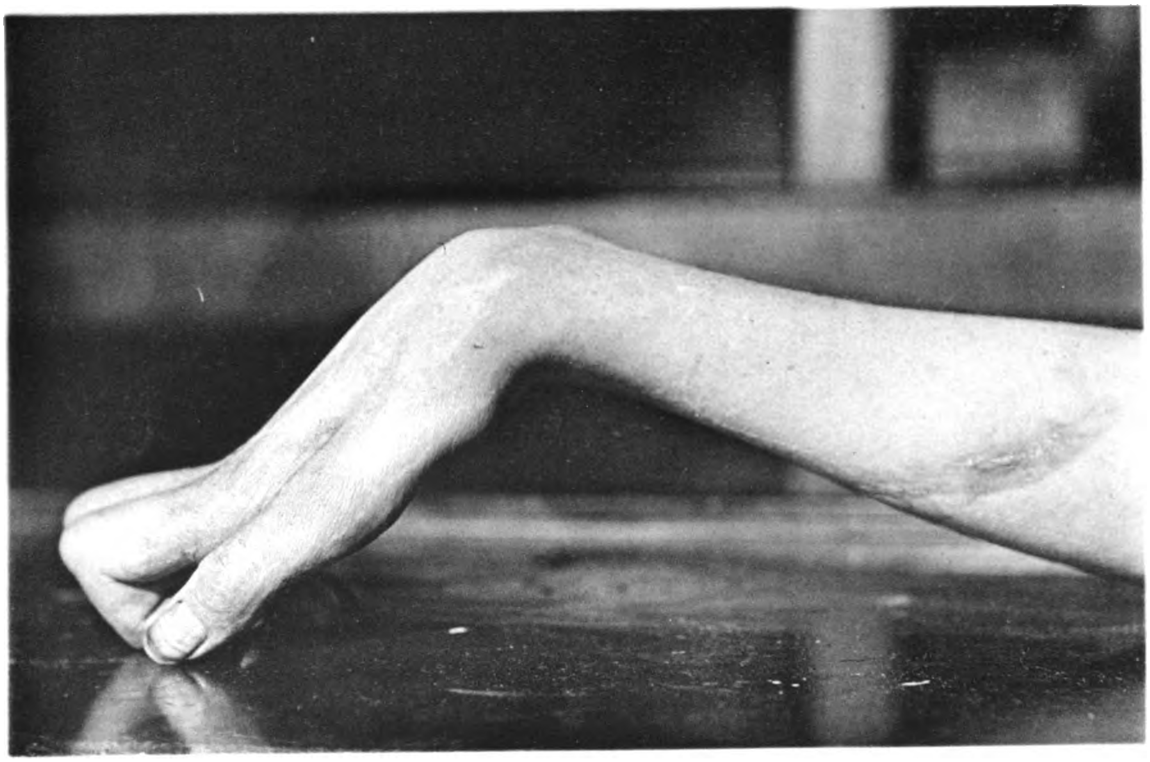

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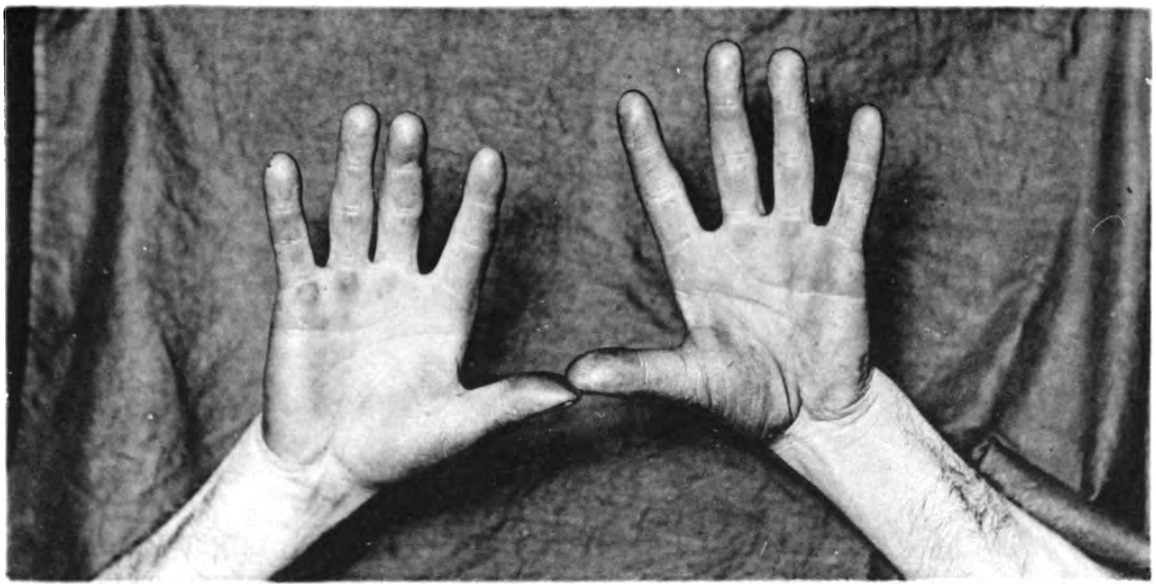

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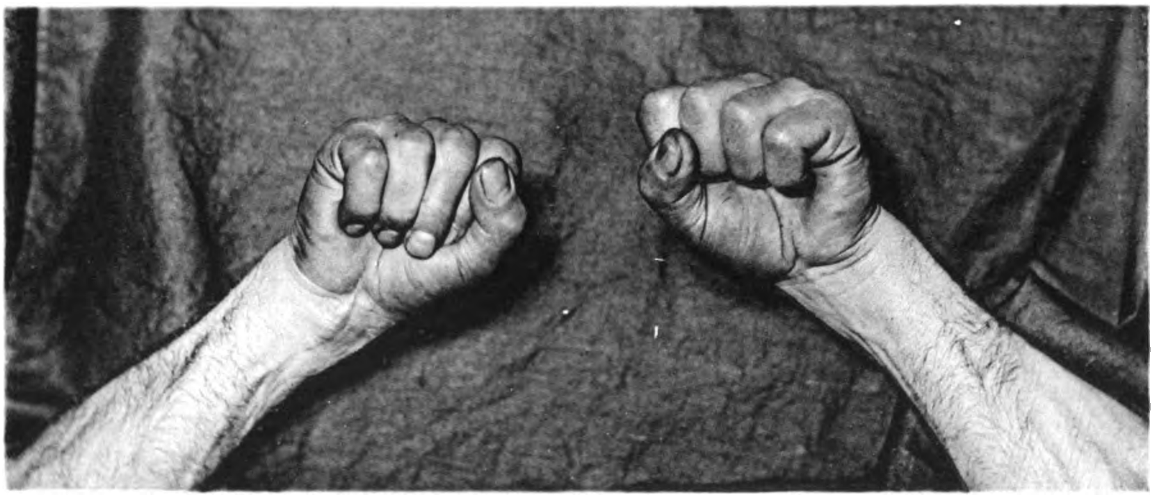

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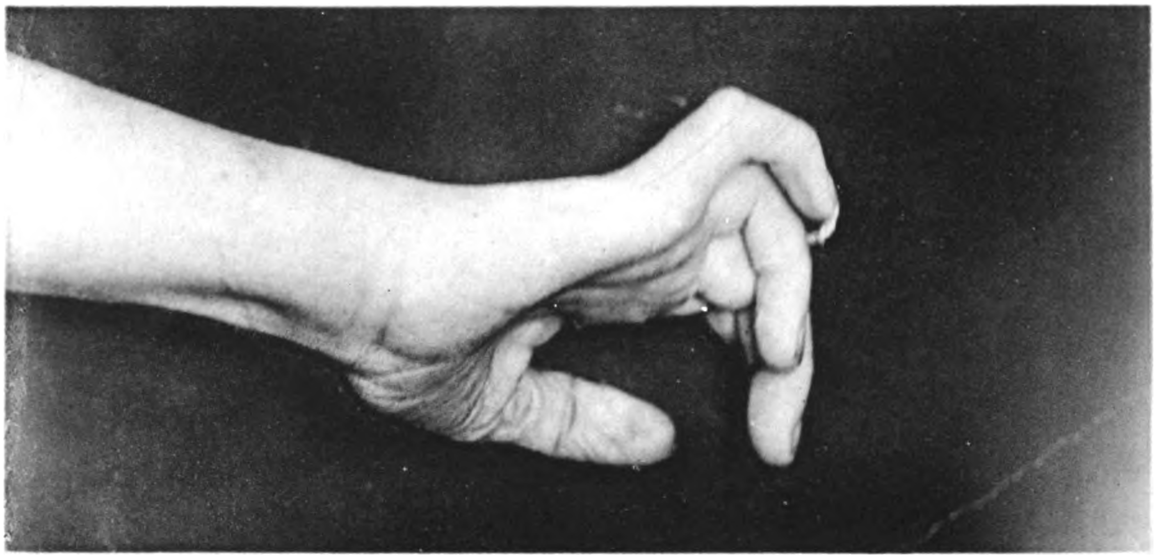

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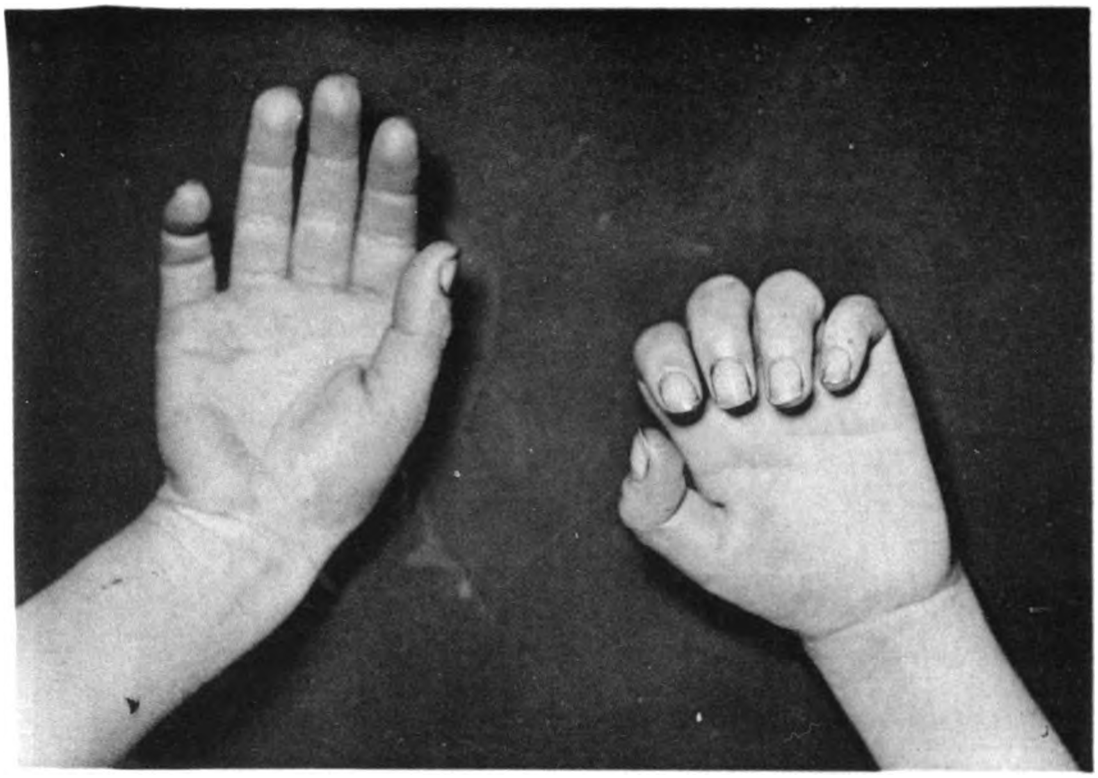

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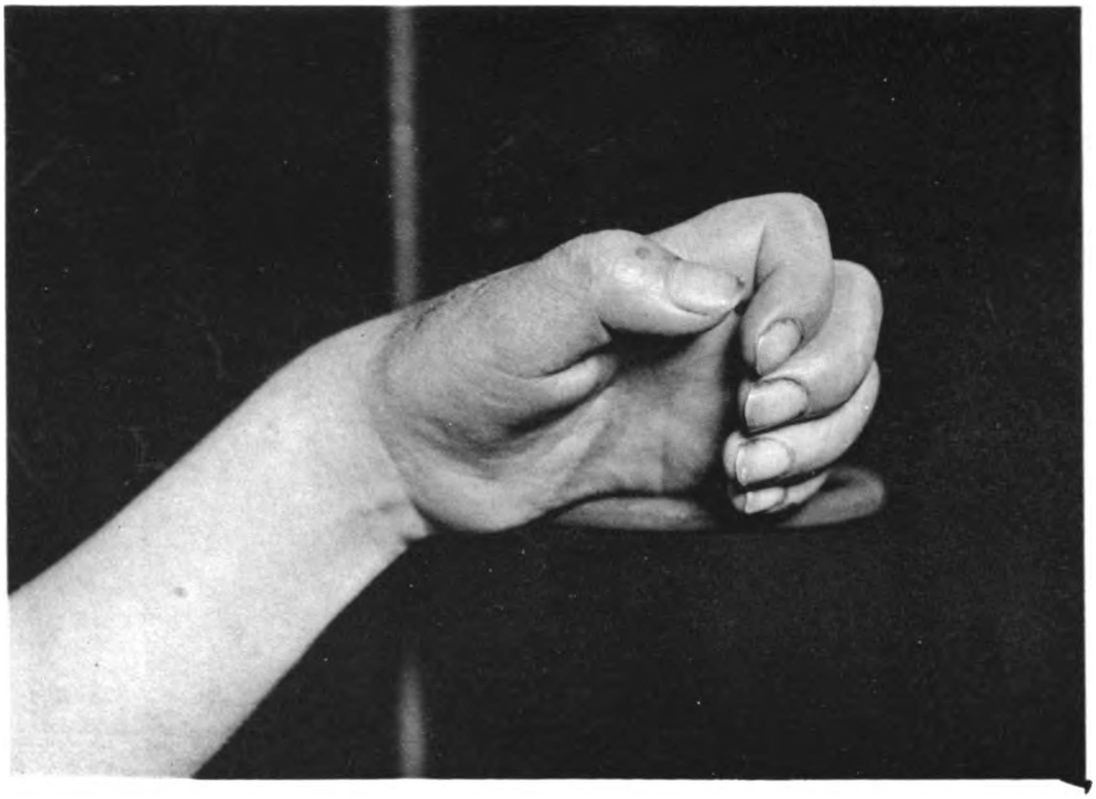

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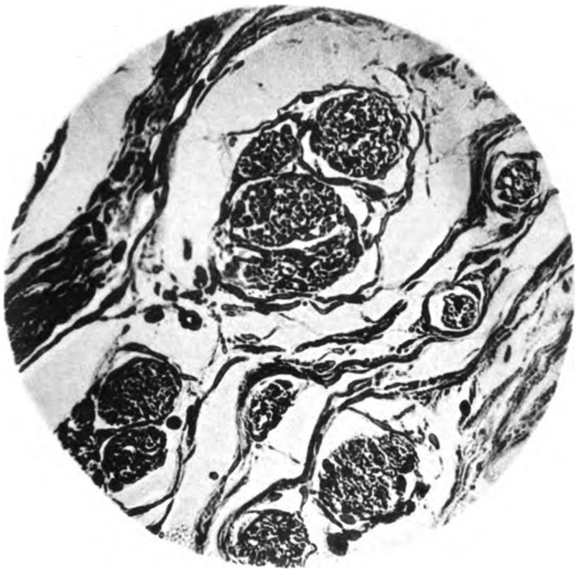

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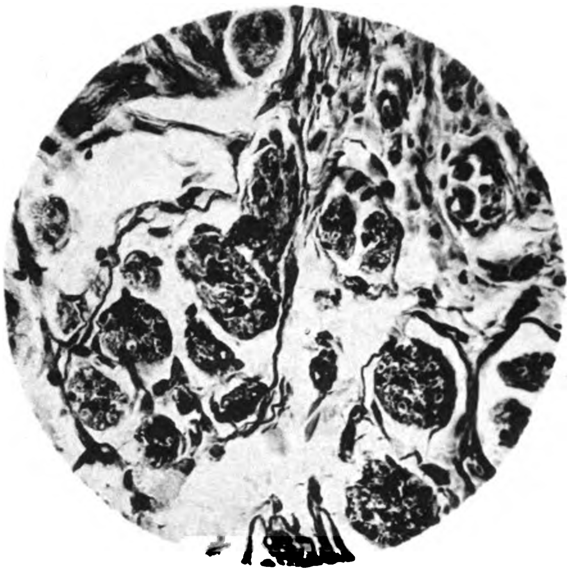

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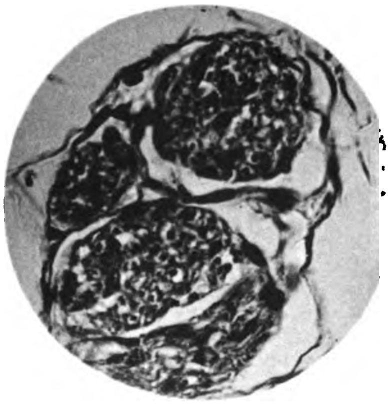

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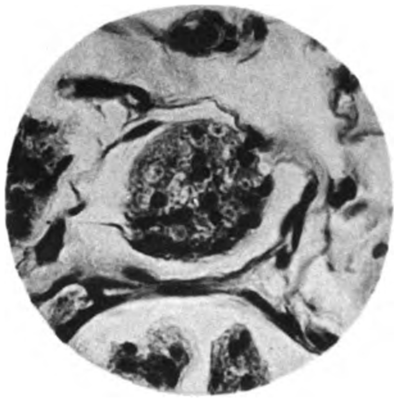

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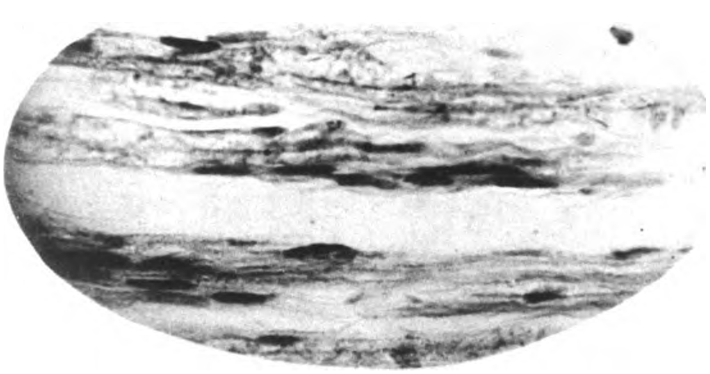

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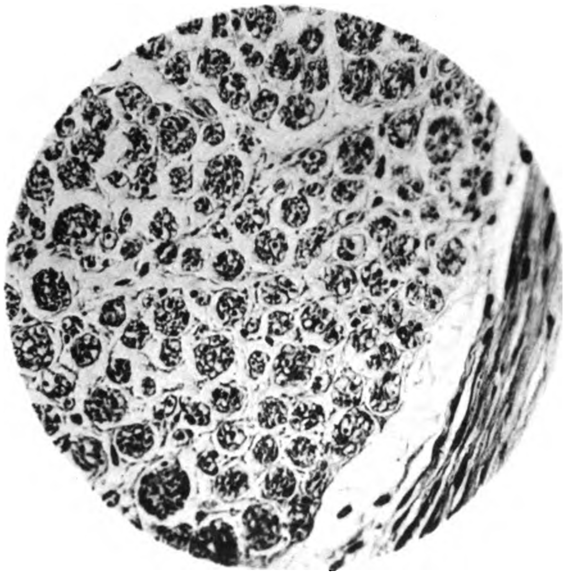

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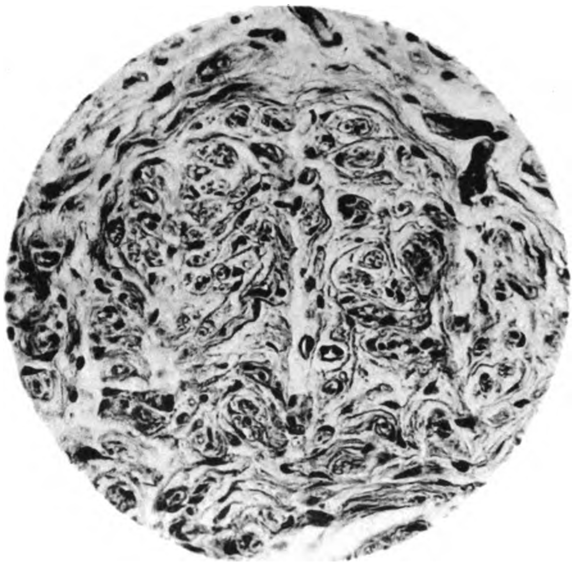
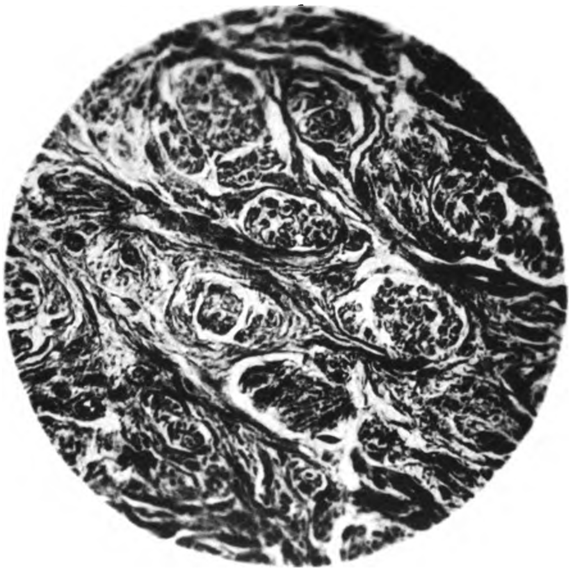


Fig. 3.



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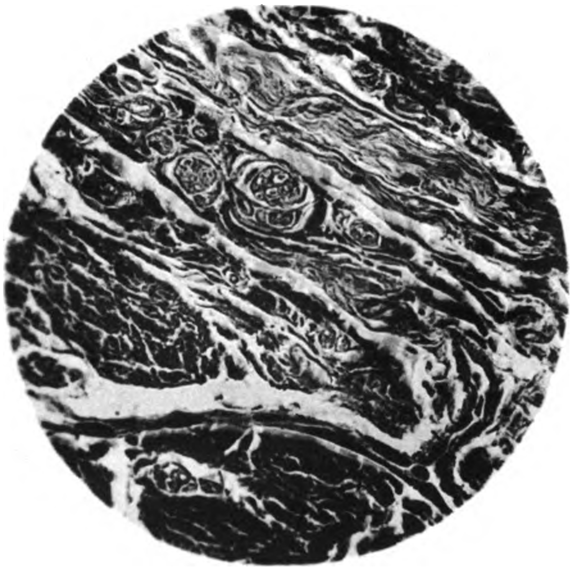

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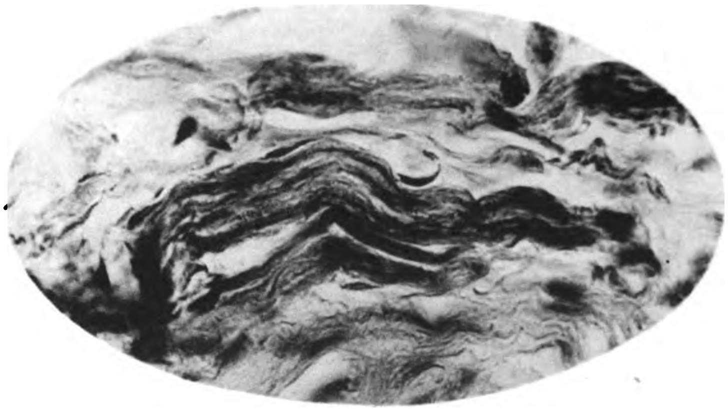

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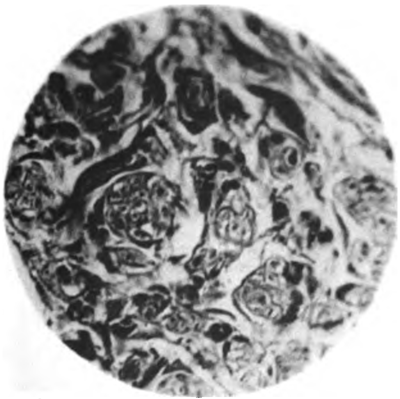

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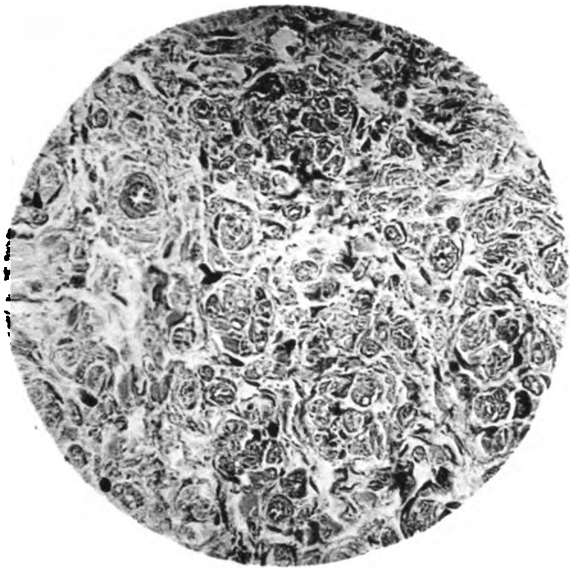

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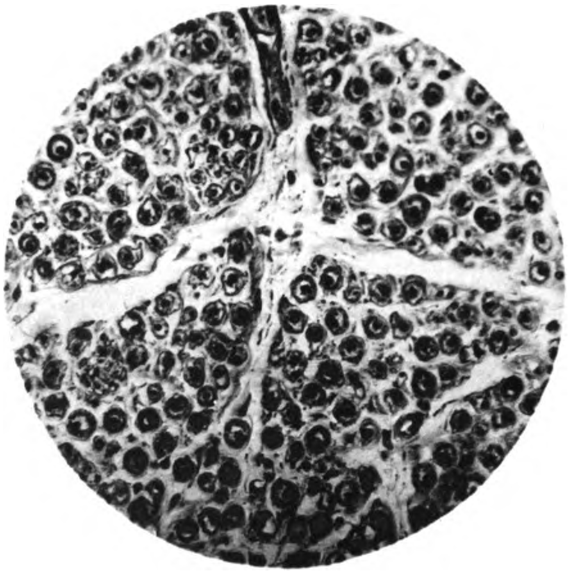

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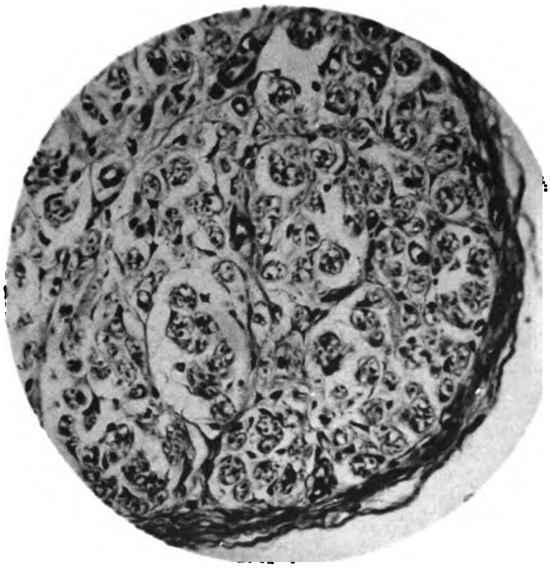

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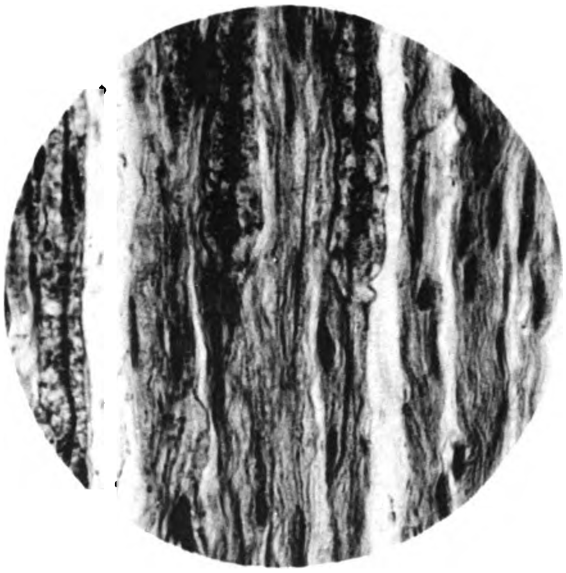

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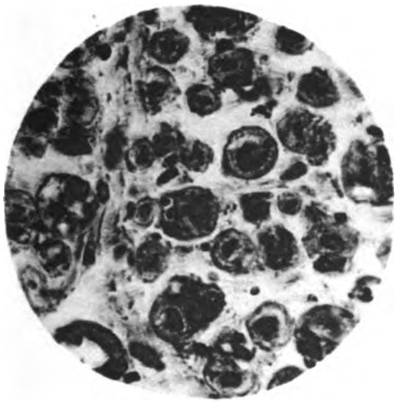

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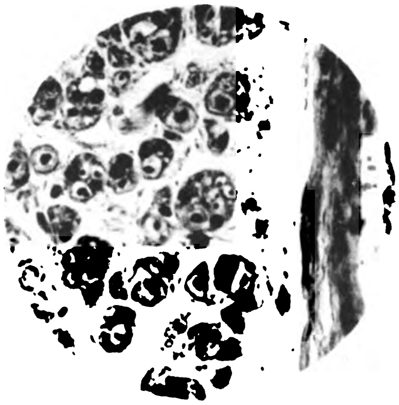

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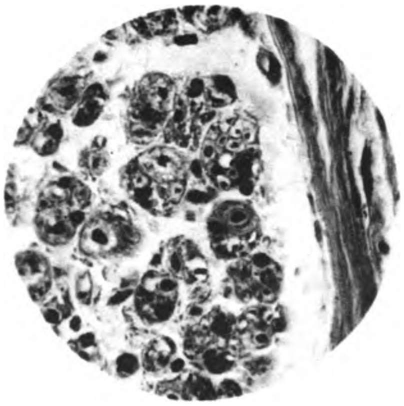

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